VOL. CLXIII, No. 5 MAY, 1922 No. 602

THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES

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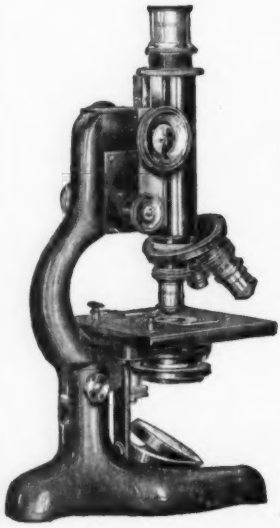

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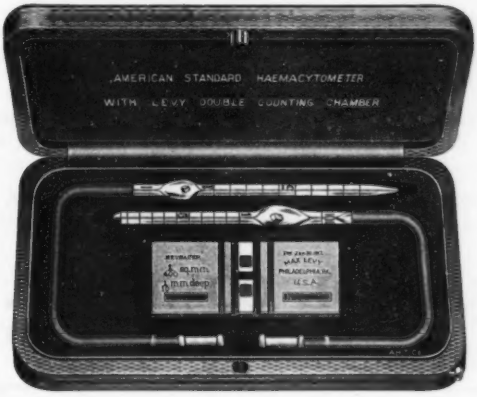

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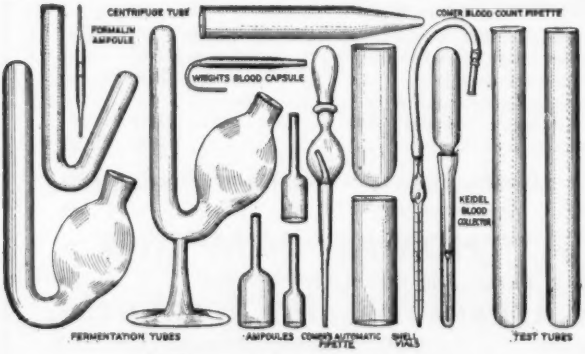

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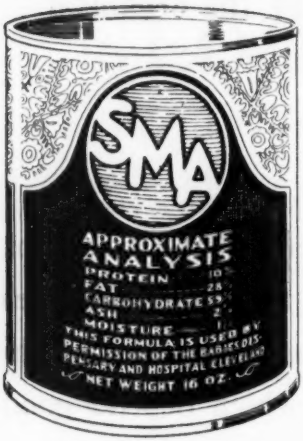

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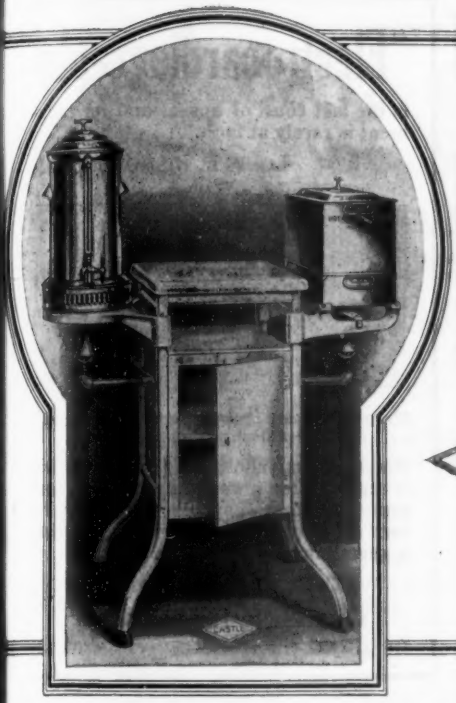

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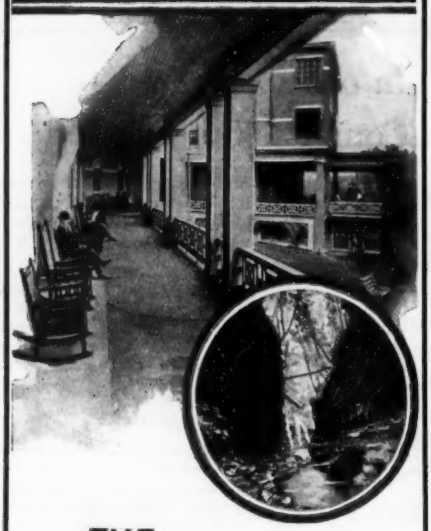

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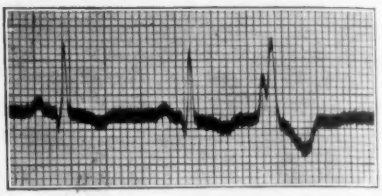

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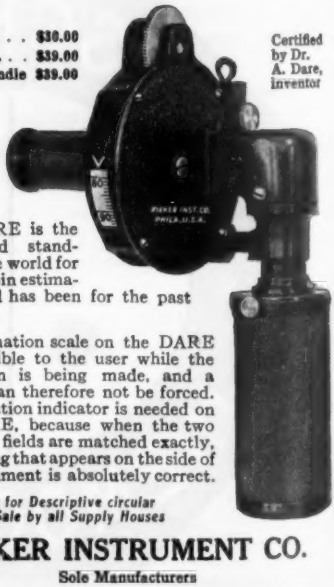

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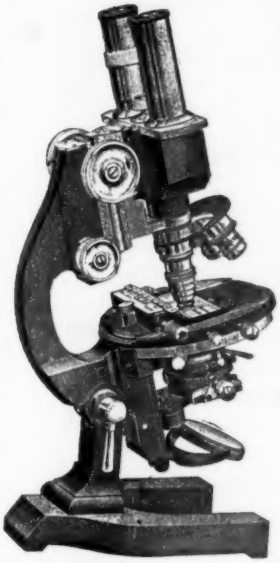

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The dates for the next two examinations of the **NATIONAL BOARD OF MEDICAL EXAMINERS** are as follows:

Part I and II, June 19, 20, 21, 22, and 23, 1922.
Part I and II, September 25, 26, 27, 28, and 29, 1922.

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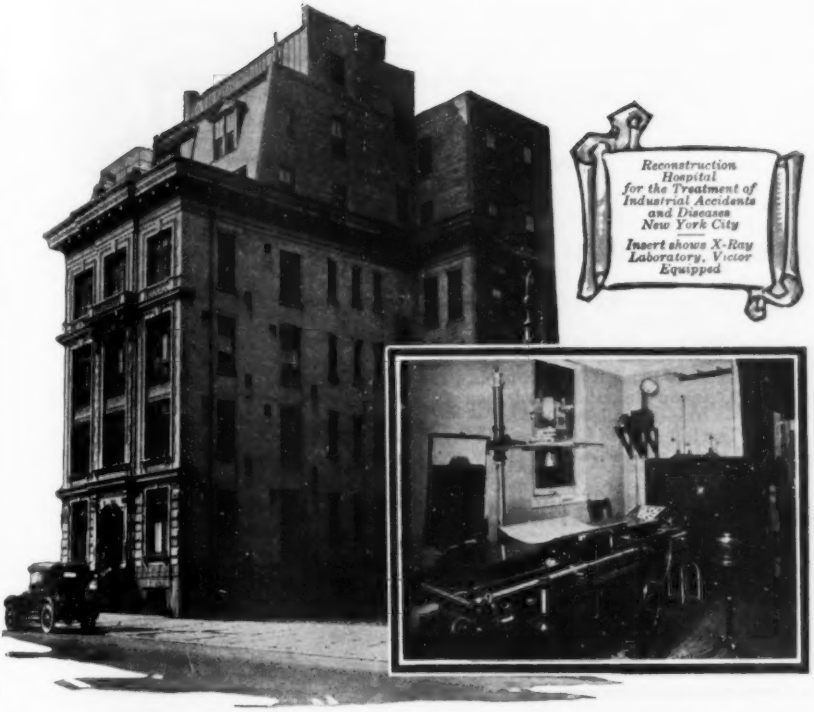

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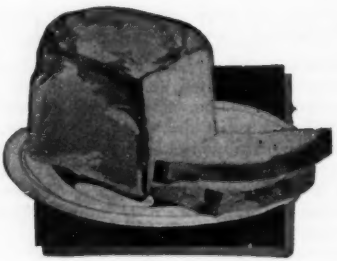

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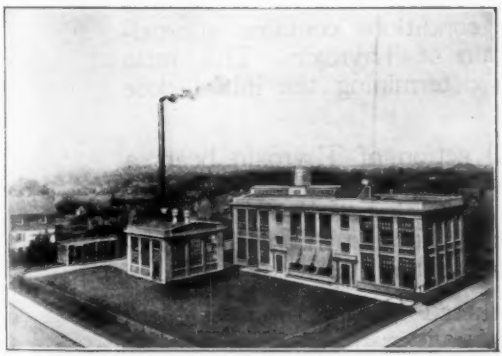

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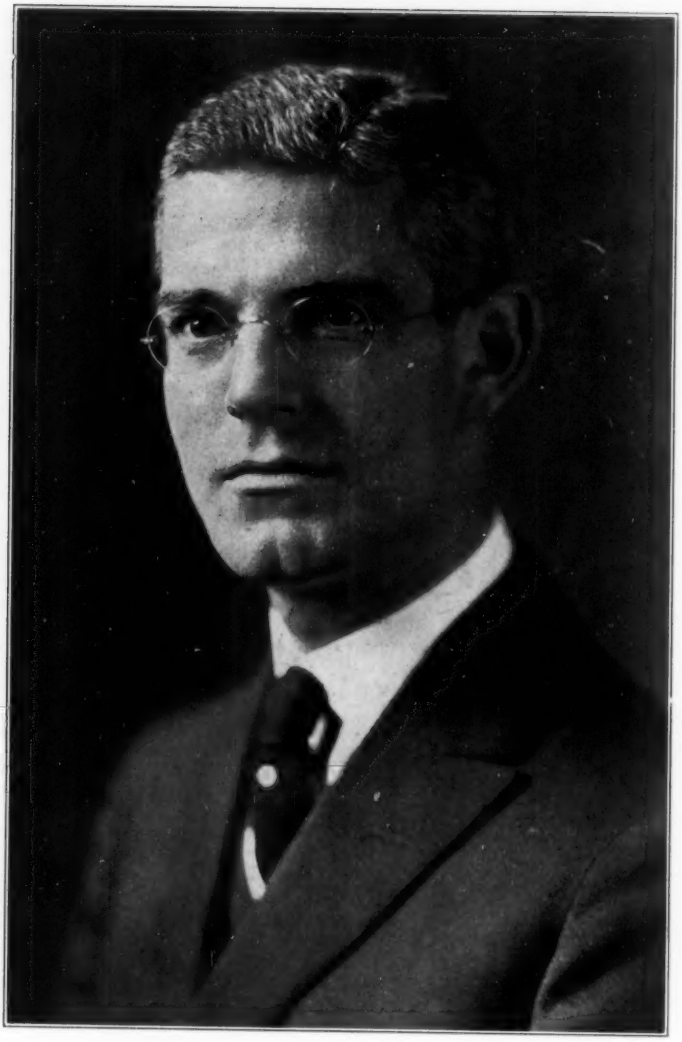

Geo. Morris Pierce

GEORGE MORRIS PIERSOL, M.D.

Editor of the American Journal of the Medical Sciences

May, 1911——April, 1922.

With the publication of the April number of the American Journal of the Medical Sciences, Dr. George Morris Piersol resigned as editor, a position which he had held for eleven years. Dr. Piersol assumed the management of the Journal when the death of the previous editor, Dr. A. O. J. Kelly, occurred in 1911. It was his constant endeavor to keep the Journal on a high plane, as regards both the literary and scientific quality of its pages, and that he achieved success is evidenced by the high esteem in which the Journal is held by the profession throughout the civilized world, and by a steady and continual growth in circulation, notwithstanding the increase in the number of very excellent periodicals devoted to special phases of medicine, in the last decade. Under Dr. Piersol's editorship the writings of the foremost men in all branches of medical science have appeared in its pages, many of these contributions marking epochs in medical progress, so that the American Journal of the Medical Sciences is today one of the most widely and frequently quoted of all medical periodicals.

It is with sincere regret that his many friends see him relinquish the work which he has conducted so admirably for so many years. However, the activities of a very busy teaching life and an extensive consulting practice require his entire attention. At the present time he holds the position of Professor of Medicine and Sub-Dean in Medicine in the Graduate School of the University of Pennsylvania, and Professor of Medicine at the Woman's Medical College of Pennsylvania. Dr. Piersol has just completed his term of office as President of the Philadelphia County Medical Society, a position which he attained not only as a result of his medical achievements but also through the universal popularity with which he is greeted throughout the city by the medical profession. In addition to these honors he is a member of the Association of American Physicians, The American Therapeutic Society, American Climatological Association and other organizations national in their scope. During the war Dr. Piersol was in active service for nearly two years. In the A. E. F. he served as Chief of the Medical Service of U. S. A. Base Hospital No. 20, later as temporary commanding officer of the same organization and subsequently as corps consultant with the rank of Lieutenant-Colonel. Dr. Piersol has many years of activity before him and there can be no question that the future will be full of great possibilities for one of his ability and talent. The American Journal of the Medical Sciences extends to Dr. Piersol its best wishes for a long and most successful career.

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

MAY, 1922

ORIGINAL ARTICLES.

IMPENDING AND REAL GANGRENE ASSOCIATED WITH DIABETES; CORRELATION OF MEDICAL AND SURGICAL EFFORT.

By Bertram M. Bernheim, M.D., F.A.C.S.

BALTIMORE, MD.

(From the Surgical Clinic of the Hebrew Hospital, Baltimore, Md.)

It is well known that gangrene of the extremities is a fairly frequent complication in diabetes; not that the condition of diabetes itself necessarily gives rise to gangrene, but that in individuals suffering from this malady there is usually to be found an associated generalized arteriosclerosis which, together with the recognized lowered resistance of the tissues to infection, may be said to prepare the field for those circulatory disturbances of the extremities that eventuate in gangrene.

At the same time it must be admitted that fundamentally the diabetes controls the situation in so far that most of those who come to grief with gangrene are found either to have neglected the general condition or are sufferers from it in such intractable form that dietetic and therapeutic measures for its relief have been unavailing. At least this is so in my experience. It appears that the basic element dependent upon control of the diabetic condition is not so much a cessation of further development of the arteriosclerotic process in the extremity bloodvessels as it is a raised tissue resistance to infection and to the withstanding of the ischemia associated with occluded arteries; for in most cases that have come under my observation a halting of the arteriosclerotic process is of comparatively minor importance, since it has already proceeded to the point

of almost total occlusion of the main terminal bloodvessel.[1] This leaves the limb to get along as best it may, with such collateral vascular channels as might have developed coincident with the gradual occlusion of these main vessels. The crux of the situation must therefore lie in the ability of the tissues to survive with a greatly diminished blood nourishment, and it is this ability which seems to be influenced by the diabetes.

That this is true is proved, I think, by the fact that in gangrenes other than those associated with diabetes it suffices in general to consider and treat the local condition alone, and if one is able to reëstablish the circulatory balance in a limb of precarious circulation, as is very frequently possible by means of rest, baths and gentle massage, the use of the electric vibrator and such other measures as one may employ in these difficult conditions[2] a successful issue may be expected. Not so in diabetes. Not once but many times have all my efforts to restore the circulatory balance gone to naught until the underlying condition could be brought under control. I refer particularly to those cases of only impending gangrene, cases which have not progressed to the stage of actual tissue death and where prompt measures might be expected to prevent it.

But in a way the same thing holds true for those who have an actual gangrene in that amputation will more than likely end disastrously, as is well known, unless at the time of operation the patient is sugar-free, and his acetone, diacetic acid, blood-sugar and carbonate findings have been brought into line. Or a better way of putting it would be to say that a patient's chances of surviving operation appear to be increased just in so far as his underlying diabetic malady is brought under control. It follows, therefore, that surgeons would do well to call to their aid physicians skilled in the treatment of this difficult disease, for it requires a special order of knowledge to deal with its various manifestations, a knowledge not usually possessed by surgeons.

This was forcibly brought home to me by a case (Mr. J. W.), which came under my care some years ago, of a man, aged sixty-eight years long a sufferer from diabetes, whose bloodvessels everywhere were of the pipe-stem variety. He had been under the constant supervision of Dr. E. J. Leopold, and in spite of occasional lapses had been carried along most successfully for a number of years, even to the point of surviving a desperate pneumonia. One winter, for some unaccountable reason, he became obsessed with the idea that he needed no further medical supervision. Being a hard

[1] That is the main vessels of the lower leg and foot. It often happens that pulsation is felt in the popliteal artery, but invariably it is found to be one-half or three-quarters occluded by the sclerotic process. So the volume of blood passing through it must be very small.

[2] Pain in Threatened and Real Gangrene of the Extremities; Its Relief, AM. JOUR. MED. SC., 1922. **163,** 517.

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drinker he indulged immoderately and totally neglected his usual dietary precautions—and with the inevitable result. When I saw him he had what looked to be a simple infection of his left great toe. Dr. Leopold was again in charge, but the patient's attitude was bad and his medical adviser was having poor success.

I started out with the usual conservative measures of rest and moist, warm boric dressings, but the tissue broke down in spite of them. I then provided adequate drainage, but the tissues seemed to have little resistance, and although there was no pain at all connected with the affected area, more destruction ensued, and it was not long before the terminal joint was invaded. Dr. Leopold thereupon redoubled his efforts. Rigorous diet was enforced under adequate supervision and everything possible was done to stave off what looked like a spreading infection with gangrene. Dr. J. M. T. Finney saw the patient in consultation and advised that he be put to sleep, the joint opened, thoroughly cleaned out and all sloughing material removed. It was with a hopeless feeling that his advice was followed.

Just before this was done it was noted that the sugar content of the patient's urine was decreasing. Coincident with this it was further observed that while the roentgen-ray showed definite bone destruction in the joint, the surrounding tissue appeared to be taking on renewed vitality and that the inflammatory area had ceased to spread. The operation was carried out under nitrous-oxide gas anesthesia. For a few days the whole foot looked precarious, but actual gangrene did not supervene. After a while the condition seemed to improve some as the general condition of the patient began to respond to treatment. Shortly thereafter the diabetic process yielded, and following this the toe healed. The patient lived a fairly active life for several years after this, finally succumbing to a second attack of pneumonia.

I cite this case because it is a most unusual one and is a striking example of successful coöperation of surgical and medical effort. The whole period of surgical treatment was most tedious, and consumed four months.

Another case, equally striking was that of an elderly man, Mr. H. H. (a patient of Dr. Samuel Wolman), who also had long been a sufferer from diabetes. Always a difficult patient, he would at times go on a veritable carbohydrate debauch, and it was at the conclusion of one of these, in the spring of 1920, that he began to have pain in his right leg. This grew worse steadily until it became so acute and constant that it was agonizing for him to walk. Sleep was out of the question.

When I saw him, some two or three weeks after the onset, there was already present a slight but none the less definite atrophy of the calf mucles of the affected leg. When the man was on his feet the veins of his right leg stood out like whip-cords while the entire

skin from the knee down assumed first a fiery red color, and then as he continued standing a purplish, ominous-looking dusky red. I have noticed this remarkable phenomenon many times in cases of threatened gangrene, and have been at a loss to explain it. The pain that accompanies it is excruciating. It looks as if the filled, tense veins would burst, and one cannot escape the feeling that the contained blood is surely obstructed in its outflow. Yet there is no obstruction demonstrable, for the moment the patient lies down the whole picture disappears, and if his leg is elevated a bit it assumes a pale, cadaveric appearance with great rapidity.

It looks rather as if at certain stages of a failing circulation in the extremities the innervation of the vessel walls becomes deranged to such extent that with the patient in the upright position there is a total loss of tone, with the resultant vein bulging with stagnant blood and the generalized phenomenon as noted.[3] This view is further supported by the fact that the affair may be purely temporary; as the circulatory balance is reëstablished by appropriate treatment the phenomenon becomes less and less pronounced; the pain on standing decreases, and finally the leg becomes normal in appearance both upon standing and lying down. In other words the vascular innervation once more becomes operative and the vessels regain their normal tone.

This is well illustrated by the story of the patient in question, as is my earlier statement that little can be accomplished without the physician's aid. I insisted immediately that Mr. H. remain in bed and be entirely off his feet. He was given the electric vibrator, hot and cold plunges to the foot and leg and such other measures as seemed indicated.[4] As the patient was in his own home the treatment was difficult and the dietary precautions nullified by his wilful excesses. His whole foot was exquisitely sensitive, and as the days progressed the picture as noted above became so exaggerated that finally I insisted that he go to the hospital for a final though, as it appeared, hopeless trial at saving the limb.

At the hospital the unexpected happened. Rigid dietary precautions were enforced, and within seventy-two hours the sugar in the urine began to clear while the man's whole aspect took on a different character. His blood sugar was 0.164 per cent. The electric vibrator, which is nothing but the gentlest form of massage, was carefully used, hot and cold plunges were regularly instituted every four hours, the leg was kept warm at all times, and in addition the patient was given a course of Ringer's solution.[5] It was not long before the pain began to subside. To make a long story short the whole picture cleared to such an extent that a few weeks later the

[3] I lay great stress upon this phenomenon in the diagnosis of threatened gangrene.

[4] Pain in Threatened and Real Gangrene of the Extremities; Its Relief, AM. JOUR. MED. SC., 1922, **163**, 517.

[5] Loc. cit.

patient was walking about as well as ever, and he has continued to do so.

Not all cases end so happily. Only too often it is not so much a question of saving the limb as the individual's life, for while diabetes itself is quite compatible with long life, diabetes plus a gangrenous limb is in all cases an extremely serious affair. Not that amputation is such a desperate ordeal in itself, but that any operative procedure of whatever magnitude is of serious import in the case of diabetes, the degree of seriousness depending for the most part apparently upon the state of carbohydrate metabolism derangement.

By way of illustration, I wish to cite three cases, each of which teaches a somewhat different lesson, though fundamentally all of them illustrate the close interrelation of surgery and medicine required for the proper handling of such cases.

The first is that of Mr. M. S., aged sixty years, a patient of Dr. T. B. Futcher. Long a diabetic, he arrived in Baltimore from the South in a profound state of acidosis. Some two or three weeks previous he began to have a soreness in his right foot, for which his medical adviser prescribed hot-water bottles. Several superficial burns on the toes resulted, and after that the dorsum of the foot became red and inflamed, and reddish streaks made their appearance above the ankle. It was then that he came to Baltimore.

Upon his arrival, April 2, 1921, he was critically ill, vomiting frequently. His urine was loaded with sugar, 2+ per cent, and also with diacetic acid and acetone, +++. His blood sugar was 0.25 per cent and his blood carbonate 39 vol. per cent.[6] His foot was obviously infected, and it seemed to have an accumulation of pus just under the skin of the dorsum, while two of his toes were already gangrenous. There was, however, no outspoken lymphangitis, and the patient's temperature was hardly elevated. So in view of his precarious general state, surgical intervention was postponed until medical measures at least could be gotten under way.

Within a few days the toxic symptoms began to subside, so that it was possible to incise and drain the dorsum of the foot. The operation was done under local anesthesia with the patient in his bed. Quantities of foul-smelling, grayish-black pus, such as is characteristically found in the tissue destruction of gangrene, were released. Following this the whole dorsum of the foot gradually became gangrenous and at each dressing that part which was obviously destroyed was removed. The two toes were removed in the same way, and as a third toe wilted it too was removed—piecemeal.

It was necessary to do this, I felt, because the accumulation of necrosed and sloughing material, with its accompanying foul-smelling liquefaction, was so great that to leave it meant that a certain amount of absorption of toxic matter must result. To have removed

[6] I am indebted to Dr. Louis Sacks, resident surgeon at the Hebrew Hospital, for much aid in the preparation of this article.

the foot—as was obviously indicated— was out of the question at this time, because the patient's general state remained so desperate as to preclude giving him an anesthetic or carrying out any operation of magnitude. But we were particularly fortunate in this case,[7] because the individual in question never suffered the slightest pain from his rapidly decaying foot. This was one of the most remarkable cases in this respect I have ever encountered. Thus by keeping well away from the line of demarcation, which was progressive, all excision of tissue was accomplished without pain and without anesthesia of any kind.

Under the constant watchfulness of Dr. Futcher, Mr. S. gradually improved. His urine revealed less and less sugar until, weeks after his admission, it finally became sugar-free. His acetone and diacetic acid, however, were very refractory, being +++ for the acetone and + for the diacetic acid. It seemed impossible to get his blood sugar below 0.21 per cent, in spite of repeated starvation days and the most rigidly careful diet on other days.

During these trying weeks there was the widest possible opening in the foot for drainage, the skin, subcutaneous tissue, extensor muscles and tendons having been removed. But the interosseous muscles were becoming affected and sloughing material was constantly oozing up between the metatarsal bones. It then occurred to me that even though the patient's temperature was running about normal, absorption was going on nevertheless, and that this was the reason for the failure of urinary and blood findings to approach normal. Dr. Futcher and I discussed this possibility and the proposition that as long as the affected leg remained unamputated the diabetic condition of the patient probably would not show further improvement. I must admit that, surgically speaking, the man's wounds were so wide open that absorption of any serious surgical significance seemed out of the question. My only ground for thinking that there was any absorption at all was merely the fact that the most intensive efforts of the medical men to improve the diabetic condition after it had reached a certain point were without avail. Our combined experience, however, in regard to this matter was rather meager, and the literature contains little or nothing concerning it.[8] It seemed a marvelous opportunity to shed some light on this point by proceeding with the amputation—and the temptation was great—but the patient's condition was such that it would have been unwise to carry out any operation without exhausting every possible means of bringing his laboratory (blood and urine) findings to normal. We therefore continued our

[7] The gangrenes of diabetes are more prone to be of the painless variety than other gangrenes, though just why this should be I do not know.

[8] Ordinarily, if a patient is absorbing from a surgical wound, one feels that the drainage is insufficient and that this will be manifested by pain, swelling and elevation of temperature.

efforts in this direction even though the gangrenous process continued to advance. I might add that the circulation in the affected leg was quite satisfactory, the patient had his normal femoral and popliteal pulses, and that such granulation tissue as formed bled with remarkable ease. In other words the spread of the gangrene was not dependent upon a circulatory failure but obviously upon a lowered resistance of the tissues to infection and to ischemia. Lest there might be some skepticism on this point, I would add that not only was the circulation quite satisfactory, but there was no edema of the foot, ankle or leg which might have interfered with a circulation that was adequate. But toward the seventh week under our care the sole of the foot began to redden. A little later it became obvious that the process had broken through the plantar fascia from above (as was to be expected), and if prompt measures were not taken a fulminating gangrene might result. This, of course, was to be avoided at all hazards. At this time the urinary and blood findings were as follows:

May 18, 1921. Urine: Glucose, 0.7 per cent (14.7 gm.); acetone, +++; diacetic, +; albumin, +. Blood sugar, 0.24 per cent.

That is they still had not reached normal. The opportunity to discover the relation of absorption from gangrenous tissue to continued carbohydrate derangement in so far as a single example could teach was within our grasp. We had played fair with the patient from an actual surgical standpoint by carrying him along without operation until his leg actually began to threaten his life.

Therefore, on May 19, 1921, under nitrous oxide gas and some ether, a hurried amputation was done at the midcalf. The patient reacted very well, and, with the exception of one small area on the outer side of the stump, the wound healed without difficulty. As we had hoped, the postoperative course of the diabetes justified fully the view held that the failure of the carbohydrate derangement to yield entirely to treatment was due purely to the absorption taking place. At least there is no other explanation for the fact that within about two weeks after the operation, June 14, 1921, the urinary findings came down to normal. The blood sugar dropped to 0.20 per cent and continued to decrease, reaching normal one week before discharge from the hospital, July 13, 1921, some three and a half months after his admission.

At this time he was on an extremely liberal diet. Daily diet the week of discharge from the hospital was as follows:

Morning: Lister biscuits, 2; peach, 1; eggs, 2; milk, 270 cc; coffee, 250 cc; butter, 10 gm.

Afternoon: Orange, 100 gm.; broth, 200 cc; beef, 100 gm.; squash, 150 gm.; tea, 200 cc; cucumber, 100 gm.; potato, 100 gm.; lister biscuit, 2. Ice cream: Milk, 150 cc; cream, 160 cc; saccharine, $\frac{3}{4}$ gr.

Evening (supper): Cottage cheese, 50 gm.; beef, 100 gm.; squash, 150 gm.; tomato, 75 gm.; lettuce, 25 gm.; milk, 300 cc.; coffee, 250 cc; lister biscuits, 2.

His general condition was all that could be desired and his carbohydrate tolerance had actually been raised to really respectable limits.

This case, then, is an illustration of the principle that in certain instances our efforts must be directed not so much toward saving the limb as saving the patient's life, and that even this at times is most problematical.

For example, just recently I had under my care a woman (Mrs. K.), for many years a sufferer from diabetes, who began to have trouble with her right leg. She was seen by Dr. Helfgott, who advised that she come to the hospital for treatment. His advice was ignored and he lost sight of her for some three months. At the end of that time the patient again came under his observation, but by that time her whole right foot had become gangrenous.

I saw her in consultation April 8, 1921, and had her sent to the hospital immediately. The patient's whole foot was decayed, the toes were hanging by shreds of tissue and in several areas where the skin was broken great quantities of pus could be expressed from the sole of the foot. The gangrenous process was gradually spreading up the ankle and the lower leg was edematous. Her urinary and blood findings at this time were as follows:

Urine: Sugar, ++++; acetone, ++++; diacetic acid, +.

Blood: Blood sugar, 0.4 per cent; blood carbonate, 48.6 vol. per cent.

Dr. Leopold, the attending physician at the Hebrew Hospital, felt that if operation could be postponed a few days it might be possible to do much in the way of improving the patient's condition and rendering the operative outcome more certain. Accordingly the foot was dressed in wet boric compresses, and from day to day the gangrenous material was removed. This patient suffered so much pain at all times that it was difficult to do much with her. For some ten days this coöperative method of medical and surgical treatment was continued and the patient showed some favorable response. The findings were as follows:

Urine: Glucose, 0; acetone, ++; diacetic acid, +.

Blood: Blood sugar ranged from 0.396 per cent to 0.48 per cent.

At this time, however, the edema of the lower leg was becoming more pronounced. It spread up the leg and definite lymphangitic streaks made their appearance chiefly along the internal saphenous vein. In other words it became obvious that the infection was progressing and that the patient's life depended upon prompt surgical interference. Accordingly a midthigh amputation was carried out. At the time of the operation the patient was in much better physical condition than upon her admission. Her tempera-

ture was down and she was practically sugar-free. Dr. Leopold and I felt that she would do fairly well after the operation, but we were disappointed. During the first twenty-four hours she was in desperate shape, but by the use of intravenous sodium bicarbonate she was tided over. For three days thereafter, April 23, 1921, she was showing improvement, and we began to feel hopeful. Her blood sugar dropped from 0.48 per cent to 0.34 per cent. Then with but little warning, some twenty-four hours after this, the patient suddenly went into a coma and died.

This case is an illustration of the difficulties that may be encountered at any time in the treatment of gangrene, namely, that a gangrene which is quiescent may suddenly become fulminating no matter what the condition of the patient. Under these circumstances, of course, operation is the lesser of two evils, and the patient must take the chance.

In the case of a third patient, Mr. S., aged fifty-four years, the conditions were even more deplorable. Not only was there the diabetic condition with a fulminating gangrene of the leg present, but in addition there was active pulmonary tuberculosis of long standing with cavities in both lungs. This involved state of affairs existed when I first saw the individual, the case having been treated on the outside for several months by others. Dr. Charles Austrian was invited to take over the medical side of the case, and at his suggestion a midthigh amputation was carried out under spinal anesthesia. The operation was done as an emergency at night; such was the danger from the rapidly advancing gangrene.

The patient was a large, fat, flabby man, definitely toxic. He had been under a fairly rigid diabetic regimen for some time at home, and as a result his urine was practically normal on admission. His blood sugar was 0.25 per cent and blood carbonate 33 vol. per cent. Despite the unfavorable outlook (to our surprise and relief) he stood the operation unusually well. With the exception of an annoying hiccough, that persisted for about forty-eight hours, his convalescence was uninterrupted. His carbohydrate metabolism was rapidly controlled, with the result that prior to his discharge from the hospital his diet was almost as liberal as that of a normal individual; his urine was sugar—, acetone—, and diacetic acid-free; his blood sugar was 0.117 per cent and blood carbonate 45 vol. per cent. His carbohydrate tolerance had been raised to really respectable proportions.

These various cases are illustrations of what may be accomplished by closely allied medical and surgical forces when arrayed against a really dangerous condition. I have taken particular pains to emphasize this feature because it has been my experience that physicians tend to handle the surgical complications of diabetes too much by themselves, thereby frequently losing the opportunity for constructive measures. This is the one side. On the other

side I find that the surgeon, when once he is consulted, is too prone to disregard the medical phase of the situation in his efforts to overcome the surgical complaint. How much better it would be for all concerned if there were an intelligent coördination of effort from the very start.

THE PREVENTION OF SIMPLE GOITER IN MAN.[1]

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To understand why anyone should undertake a goiter survey of a whole community for the purpose of establishing a principle of prevention by a simple and practical method, it is necessary to study the literature of goiter with this idea in view. For the literature, while rich in statements regarding the distribution of goiter, the pathology of the thyroid gland, methods of medical and surgical treatment, hereditary tendencies and etiology, has little indeed to offer regarding the *prevention* of goiter.

A survey for merely determining the incidence of goiter in the different localities and cities of this portion of the Great Lakes basin would have been unnecessary. There is an abundance of scientific data giving in general the geographic distribution of endemic goiter throughout the world. Surveys of various communities in Europe have been made and the scientific data of the last century has so emphasized the sociologic and economic importance of endemic goiter, cretinism and deaf-mutism that national commissions have been appointed by some of the countries of Europe to study this problem for the purpose of finding some method of relief.

For ten years preceding the beginning of our work in Akron, Marine and Lenhart, working in the department of experimental medicine of the Western Reserve University, had been showing the ease with which endemic goiter could be prevented. The results of laboratory experiments and demonstration in animals, however convincing, must be applied to man for final proof of their prophylactic or therapeutic value. The prevention of goiter in man was yet to be proven. Therefore, with Dr. David Marine, I undertook to establish in man the applicability of the work of Marine and Lenhart as summed up in their statement that "simple goiter is the easiest of all known diseases to prevent."

Definition and History of Endemic Goiter. The term goiter means hypertrophy of the thyroid gland. The term as used in this paper refers only to what is known as *simple* or *endemic goiter* and does not include the so-called exophthalmic goiter.

[1] Presented as a thesis for the degree of Master of Arts in Medicine, Western Reserve University, June, 1921.

The incidence of simple goiter is so high and so continuous for generations, in certain districts of the world where all kinds of domestic animals as well as humans are involved, that it has come to be considered as characteristic of or endemic in that district.

The study of the history of this disease is like studying the history of the human race. The Arthorva Veda, an ancient Hindu collection of incantations dating from 2000 B. C., contains extensive forms of exorcisms for goiter. Caesar mentions the frequent occurrence of big neck as one of the peculiar characteristics of the Gauls. The origin of the term cretin shows the familiarity of the early Romans with this disease. They originated this expression of contempt by calling the myxedematous idiots Christians. The Swiss physician Paracelsus (1493–1541) was the first to emphasize the relationship between goiter and cretinism, and the earliest positive information concerning the latter disease dates from this author. In 1793 appeared Fodere's essay on "Goiter and Cretinism in the Maurienne and Aosta Valley," and in 1800 his *Treatise on Goiter and Cretinism*. During the last century there have been numerous publications on endemic goiter and cretinism, one of the most exhaustive of which is by A. Hirsch, in his study of the *Historical and Geographical Relations of Goiter*.

About the middle of the last century the governments of the European countries began to see the economic and sociologic importance of this problem. In 1848 the Sardinian government appointed a commission to study the cause of endemic goiter and find some method of relief. In 1864 the French government appointed a similar commission, which reported in 1874 that at least 500,000 people in France were suffering from goiter and that there were over 120,000 cretins and cretinoid idiots. This commission seemed to establish as a scientific fact the popular idea that goiter is a water-borne disease. In 1908 Switzerland created a goiter commission, and since then Italy has created a similar commission to study the cause and prevention of endemic goiter.

Distribution. The extent to which goiter prevails throughout the world is seldom appreciated. Few countries are free from endemic districts, and we find the so-called sporadic cases of goiter in every section and among every nationality in the world. But there are localities in which the incidence of goiter is so extremely high that they have been known for years as endemic goiter districts. The best known of these districts is in southern Europe, or, more specifically, the Alps mountain region, comprising southeastern France, southern Germany, all of Switzerland, northern Italy and southern Austria. In Asia practically all of the Himalaya district is an endemic goiter belt, with a very high incidence in northern India and parts of southern and western China and eastern Mongolia. In South America goiter is endemic throughout most of the Andes region, with probably the highest incidence of both goiter and

cretinism on the Peruvian plateau and in parts of western Brazil. In North America goiter is endemic in the whole of the Great Lakes' basin, in the basin of the St. Lawrence and in the northwest Pacific region.

In each of these large endemic regions there are localities in which the incidence of goiter is much higher than in the surrounding territory, and in such districts all of the domestic animals are affected. In some of these smaller districts the incidence of goiter has been determined with sufficient accuracy to be mentioned here. For example, as we have stated above, in 1874 the Goiter Commission of France estimated that in that country there were 500,000 goitrous people and 120,000 cretins and cretinoid idiots; statistics furnished by Kocher show that 80 to 90 per cent of the school children of Berne were goitrous; in his recent reports Klinger states that in some of the schools of Zurich, where he is carrying out methods of goiter prevention, 100 per cent of the children are goitrous. In southern Bavaria, according to the statistics of Schittenhelm and Weichardt, who base their conclusions on examinations of school children, the incidence of goiter is as high as from 77 to 89 per cent of the total population. In Switzerland and in certain provinces of Italy, France and Austria the problem of endemic goiter, cretinism and deaf-mutism has been recognized as of sufficient economic importance to demand investigation by their respective governments.

We are told that on the Gobi Desert and the plateau of Thibet the incidence of goiter is very high, and that among the various tribes of southeastern Mongolia a third of the population is goitrous.

McCarrison carried out some of his researches and made several surveys in Himalayan India. He states that in some of the villages of this section it is difficult to find a man, woman or child who is not suffering from the deformity. He estimates that not less than 20 per cent of the total population of Gilget, in northern India, suffer from goiter, and that among a population of 70,000 he found 200 cretins.

The frequency of goiter in North America has been known in a general way for more than a century. In 1800 Barton wrote an excellent monograph on the occurrence of goiter among the American Indians living along the shores of Lakes Ontario and Erie. Other goiter centers among the Indians of the Rocky Mountain States have been described by Munson. Adami pointed out the frequency of goiter in the St. Lawrence Valley, and speaks of French Canadian villages in this district in which there was scarcely a family without one or more goitrous members. Osler has emphasized the frequency of goiter in Ontario. Marine finds the disease widely disseminated all along the Great Lakes, where it occurs not only in humans but also in animals, especially dogs and sheep. In a report to the Commission of Conservation of Canada in 1918,

Shepherd states that the incidence of goiter is very high in British Columbia and Alberta, and that in some localities of these large states most of the domestic animals are affected.

Incidence of Goiter in the United States. Efforts to determine the incidence of goiter in different sections of the United States have been made but no accurate survey of a whole community had been reported previous to our work in Akron. In 1913 Clark examined 13,836 school children in eleven counties of West Virginia and found 1234 cases of goiter—9 per cent of the number examined. In Virginia the same worker examined 6432 school children and found 817 cases of goiter, or 12 per cent of the number examined. In Huntington 50 per cent of the girl students were found to be affected. In the Virginia survey less than 0.1 per cent of the goiters found were among boys.

The report of Hall of 3339 students at the University of Washington is indicative of the incidence of goiter in the Northwestern States. This writer found enlarged thyroids in 18 per cent of 2086 men whose average age was twenty years and five months, and in 31 per cent of the 1253 women examined whose average age was nineteen years and three months.

In Chicago, Olson examined 606 women and 193 men, with ages ranging from eighteen to sixty years. Among the women 18 per cent had well-developed goiters, and 7 per cent of the men were affected.

During 1917 and 1918, when so many of our young men were in camp, an opportunity was offered to determine the incidence of goiter among young men and to compare the incidence of goiter in different sections of the country. Thus from Camp Lewis, Washington, Kerr reported the examination of 21,182 recruits, with the finding of 1276 large or well-formed goiters. The percentage of unquestionable goiters compared to the number of recruits from each state was as follows:

Washington, 11 per cent.
Oregon, 8.6 per cent.
Idaho, 7.3 per cent.
North Dakota, 6.6 per cent.
Utah, 5.5 per cent.
Minnesota, 5.1 per cent.
Wyoming, 3.7 per cent.
South Dakota, 2 per cent.
Nevada, 1.1. per cent.
Colorado, 0.5 per cent.

Brendel and Helm, studying the same problem at Camp McDowell, California, conclude that goiter is endemic in Washington and Oregon. Smith, at Jefferson Barracks, Missouri, reports that in the examination of 65,507 men there were found 1074 cases of simple goiter, or an incidence of 1.63 per cent of the total number

examined. These recruits represented fifteen different central and western states. These findings only emphasize in a general way the fact that goiter may be considered as distinctly endemic in certain sections of the United States.

The Physiology of the Thyroid. In order to appreciate the principle of goiter prevention one must review briefly the biochemistry and function of the thyroid gland.

Early in the sixteenth century Paracelsus emphasized the relation between endemic goiter and cretinism. In 1825 Parry's descriptions of cases of goiter or enlargement of the thyroid gland in connection with enlargement of the heart with palpitation and exophthalmos were published. In 1835 appeared Graves's description of the clinical complex of exophthalmic goiter, with enlargement of the thyroid as one of the cardinal symptoms. Basedow's description of the same syndrome appeared in 1840. But none of these observers interpreted their findings in terms of the function of the thyroid. The first important observations of the functions of the thyroid were published in 1874 by Sir William Gull. At this time the clinical complex of myxedema (Gull's disease) was described in detail, and this clinical picture was interpreted as in some way associated with a lack of function of the thyroid.

Gull's observations and interpretation of the etiology of myxedema were confirmed in 1880 and 1881 by Kocher and Reverdin, who had observed the results of the total removal of goitrous thyroids. Kocher gave to the clinical syndrome resulting from complete thyroidectomy the name of cachexia strumipriva. Reverdin called it operative myxedema. In 1877 Ord designated the disease as myxedema, because he thought he had recognized a mucoid change in the subcutaneous tissue. Sir Victor Horsley verified the findings of these observers by his researches on experimental myxedema in monkeys. As a result of these observations, Murray and McKenzie in 1891 gave glycerinated thyroid extract to a myxedematous patient and obtained definite therapeutic results. Magnus-Levy, in 1895, showed that heat production was markedly reduced in cases of myxedema and that thyroid feeding raised it, thus establishing the essential or at least the major function of the thyroid as we know it today.

The early Greeks treated goiter by the internal administration of the ash of burned sea-sponges, not knowing that the substance was rich in iodides. Iodin was first knowingly used in the treatment of goiter by Coindet in 1820. From that time iodin was used very extensively and stood alone in goiter therapy for seventy-five years before the discovery by Baumann, in 1895, that iodin was a normal constituent of the thyroid gland. Our knowledge of the chemistry of the thyroid progressed rapidly after Baumann's discovery. In 1901 Oswald showed that the iodin is bound with the globulin and is contained for the most part in the colloid.

In 1907 Marine emphasized the fact that iodin is necessary for the normal function of the thyroid, and also in active hyperplasia of the thyroid the iodin store is reduced. The later experiments of Marine and Lenhart have established the following facts relative to the importance of iodin in the chemistry, function and histologic anatomy of the thyroid:

1. Iodin is a constituent of the normal thyroid of all animals with the ductless thyroid. As shown by their experiments on the rapidity of absorption of iodin by the thyroid, its elaboration into the active hormone and by alkaline hydrolysis, as introduced by Kendall, iodin exists in the thyroid in an *active* and *inactive* form. That is, the elaboration of the hormone goes on slowly from the inactive iodin collected from the blood. The excess of physiologically active iodin is for the most part stored in the "colloid" or globulin of the alveoli, and it is believed that colloid serves merely as the vehicle or means of storing the excess of this remarkably active substance in a harmless manner. The store of iodin then normally consists of inactive iodin for the most part in the cells and of active iodin for the most part in the colloid or thyroglobulin.

2. This store of iodin shows wide variations in any series of animals. These variations reach their maximum in the so-called goiter districts and their minimum in non-goitrous districts.

3. Further, these variations in iodin store have been shown to have an intimate relation with the histology of the gland. Thus in all species of animals with the ductless thyroid the iodin store is decreased in the hyperplasias. This decrease is proportional to the degree of hyperplasia. In mammals, *e. g.*, dog, sheep, ox, pig, rabbit, cat and man, it has been shown that normal thyroids have the highest percentage of iodin, averaging 0.2 per cent, with extremes of 0.1 and 0.5 per cent.

4. It has been further shown that as soon as the store of iodin falls below 0.1 per cent active hypertrophic and hyperplastic changes in the thyroid begin. In other words, no functional hyperplasia and therefore no goiter can develop, at least in the mammals above mentioned, if the iodin store in their thyroids is maintained above 0.1 per cent.

5. This iodin store may be rapidly and markedly increased by the administration of exceedingly small quantities of iodin in any known form and through a great variety of means, as inhalation, enteral and parenteral administration, cutaneous application, etc., and as indicated above, marked histologic changes are at the same time brought about in hyperplastic glands, namely, the arrest of the hypertrophy and the involution or return of the thyroid cells to their resting form.

The active iodin compound found in the thyroid, beginning with its discovery by Baumann in 1896, and the successive attempts to isolate it, has been known as iodothyrin, iodo-thyro-globulin

(Baumann and Roos), thyroidin (Oswald) and thyroxin (Kendall). In 1915 Kendall succeeded in isolating this iodin-containing hormone in crystalline form and has determined its structural formula. He believes it to be tri-iodo-indol-propionic acid.

In 1895 Magnus-Levy indicated that the thyroid, in some way, controlled the rate of oxidation in the tissues. He showed that in myxedema the rate of metabolism was much lowered and that by feeding thyroid the rate could be raised. Also, he was the first to demonstrate that as regards metabolism exophthalmic goiter was the opposite to myxedema. This work has been confirmed from many sources as regards experimental and spontaneous myxedema. And as regards exophthalmic goiter, it has so developed that at present the rate of metabolism is the best available basis for classification.

In a recent publication on *The Physiology of the Thyroid*, Marine states that "The thyroid has to do in some important way with internal respiration or the utilization of oxygen by the tissues. Indeed, this is the only known function of the thyroid."

The Prevention of Goiter. Before 1896 Halsted had shown that if a portion of the thyroid is removed or destroyed the remainder undergoes hyperplasia. Marine and Lenhart found that this compensating hyperplasia could be prevented if the remainder of the thyroid was kept saturated with iodin. This was true in dogs as long as at least one-sixth of the gland was left, but if more than five-sixths were removed a compensatory hyperplasia followed even though iodin was given. This important observation pointed directly to iodin as the means for the prevention of thyroid hyperplasia (goiter).

One of the first practical applications of the principle of prevention of goiter and myxedema accidentally followed the discovery of salt in Michigan and its more extensive use (as crude salt) in the sheep industry of this state at a time when the industry was being crippled by endemic goiter. This crude salt was afterward found to be rich in iodin. The first definite application of the use of iodin in the prevention of goiter on a large scale in animals was the prevention of goiter in brook trout. This disease had been the cause of much trouble and expense. The so-called thyroid carcinoma in brook trout had become so serious at many private, state and government hatcheries that the question of abandoning the industry was being discussed. An investigation of the causation and a study of methods of prevention was undertaken by Marine and Lenhart in conjunction with the Pennsylvania State Fish Commission during the years 1909, 1910 and 1911. Their conclusions as to the etiologic factors producing goiter and the practical method of its prevention were definite and convincing. The important factors which in this instance caused endemic goiter were (1) overfeeding with an artificial food and (2) overcrowding. These investigators showed that goiter

could be prevented in young fish under the same environmental conditions which produced goiter by adding a very small amount of iodin to the food or water, or it could be prevented by changing the diet and remedying the overcrowding. The results of this practical research have been far reaching.

In addition to the experimental work above mentioned the treatment of goiter with iodin at the dispensary at Lakeside Hospital had been followed for the past ten years. Also the maternity dispensary of Lakeside Hospital had not only been using iodin in the treatment of goiter but had been using it as a prophylactic measure during pregnancy. To most of the men in touch with the goiter clinic at Lakeside or the school of medicine the prevention of goiter was no longer an experiment but an accomplished fact.

Therefore at the beginning of our work in Akron the possibility of goiter prevention had been clearly demonstrated by animal experimentation, but only a very limited application of methods of prevention had been made in man. No subject in preventive medicine had a sounder or more scientific basis for its practical application to man on a large scale than the prevention of endemic goiter. Yet there was considerable criticism and opposition which had to be overcome. This criticism centered about the possible untoward effects of iodin, especially the dangers of producing exophthalmic goiter.

Etiology of Endemic Goiter. Before anyone can fully comprehend the fundamental principles underlying the method of prevention which we have used, he must have some conception of the factors causing the disease. There have been many theories as to the cause of goiter, most of which are only of historic value and will not be taken up here. At present there are a few who consider goiter as a primary disease or idiopathic enlargement of the thyroid gland.

McCarrison considers it a water-borne infectious disease, the exciting factor of which is a *contagium virum*, and suggests that it belongs to the colon group of bacteria. Shepherd, also, in his report in 1918 on the occurrence of goiter in Canada, concludes that it is a water-borne infectious disease, directly comparable to typhoid.

However, most of the scientific investigators of this country look upon goiter as a deficiency disease. Marine has been emphasizing this point since 1907. As has been pointed out:

1. Iodin is essential to the normal thyroid activity.
2. From a purely biochemical standpoint any substitution for iodin destroys the physiologic activity of the thyroid hormone.
3. From the histologic point of view glandular hyperplasia of the thyroid is due to a deficiency of iodin.
4. The physiologic action produced by thyroid extract is always proportional to the iodin content.
5. In animal experimentation if the iodin content is maintained

at or above one tenth of 1 per cent no anatomic changes toward goiter formation can take place.

These facts, with our results in preventing goiter in school girls by simply keeping the thyroid saturated with iodin, make the infectious theory at once untenable. These facts lead to the conclusion that the immediate or exciting cause of endemic goiter (hypertrophy of the thyroid gland) is a lack of iodin in the organism. This lack of iodin may be relative or absolute. The remote or fundamental cause of goiter is quite unknown.

Practical Application of the Principle of Goiter Prevention. In the practical application of the principle of prevention we chose the public schools for two reasons: (*a*) The children are in the adolescent age, the most important period in the development of goiter; (*b*) the public school group furnishes the best census of goiter in any community and makes it possible to carry out, through the school organization, the most expedient, economic and practical plan of prophylaxis and education.

In October, 1916, we explained the principle of the prevention of goiter to the superintendent of schools of Akron, Dr. H. V. Hotchkiss. He promised the full support of all the school authorities if the local medical society would sanction the work. After this idea had been explained to the Summit County Medical Association this body, in a regular session, voted to send the following message to the school board: "The idea of prevention of goiter as outlined can do no harm and may do good. We are in favor of seeing it carried out." The school board authorized the superintendent to call upon Dr. Marine and myself to make a survey of goiter among the school children of Akron and carry out any plan of prevention we saw fit.

In April, 1917, an examination for thyroid enlargement was made of all the girls from the fifth to the twelfth grades inclusive. The boys were not examined because of the relative infrequency of goiter in boys. The result of each examination was recorded on a special individual card, which on one side had space for the pupil's *name, school, age, grade* and the tabulations of four thyroid examinations. On the back of this card was space for the record of eight series of prophylactic treatments, which were recorded by the teacher giving the treatment. This goiter card was attached to the school record of each pupil and was transferred with the pupil whenever transfer to another school was made. In no other way could we have kept track of so many cases over so long a time.

The details regarding this examination and the plan for carrying out the treatment were then published. Only the resultant figures will be given here. 3872 girls were examined, with the following results:

Normal thyroids, 1688, or 43.6 per cent.

Slightly enlarged thyroids, 1931, or 49.9 per cent.

Moderately enlarged thyroids, 246, or 6.3 per cent.
Markedly enlarge thyroids, 7, or 0.2 per cent.
Among these there were 39 adenomas, or 1 per cent.

In April, 1917, the first prophylactic treatment was administered to more than 1000 girls who had elected to take it. No girl was urged and no one was permitted to take it unless she had a written permit from a parent.

In November, 1917, a second examination of all girls from the fifth to twelfth grades inclusive was made, in all 4415 cases, 1772 of which were new records. Of the 2643 old recores 764 had taken the prophylaxis during the preceding six months and 1879 had not. As was published then there was not a single case in which a normal thyroid increased if the pupil was taking iodin, while among those not taking iodin 26 per cent of those marked normal at the first examination showed definite enlargement—some already having developed moderately large goiters. Even more than a prophylactic action was shown by the results—just one-third of the "small goiters" had disappeared and one-third of the "moderate goiters" had decreased 2 cm. or more.

In November, 1918, a third examination of 4277 girls was made. In October, 1919, 5520 individual examinations were recorded, and during the entire period 9967 different girls were reported.

Effect of Prophylactic Treatment. The prophylactic treatment as carried out for the past three years in the Akron schools consists of the administration of 2 gm. of sodium iodide, given in 0.2 gm. doses daily for ten consecutive school days, repeated each spring and autumn. The general data of the pupils not taking the treatment are given in Table I, and of those taking the treatment in Table II. Only pupils who have had two or more consecutive examinations have been included in these tabulations. A considerable number of pupils, both of those who have been taking the treatment and of those who have not been taking the treatment, have been omitted because they missed one examination, although otherwise their records were complete; 2305 pupils are included in the tabulation of those not taking treatment and 2190 in the tabulation of those taking treatment.

Furthermore, properly to interpret the results, it was necessary to take into consideration the length of time each pupil had been under observation. As the prophylactic treatment was given at intervals of six months we have used this interval as the unit and grouped the pupils according to the periods each had been under observation, *i. e.*, six, twelve, eighteen, twenty-four or thirty months. The results of only three groups, those with normal, slightly enlarged and moderately enlarged thyroids, are included because the fourth group, those with markedly enlarged thyroids, is too small. A comparison of the two tables brings out striking differences between those not taking and those taking iodin. These differences are

manifested both in *prevention of enlargement*—prophylactic effect—and in a *decrease* in the size of existing enlargements—therapeutic effect.

TABLE I.—RECORD OF PUPILS NOT TAKING PROPHYLACTIC TREATMENT.

Time under observation, mos.	Normal.				Slightly enlarged.						Moderately enlarged.					
	Unaltered.		Increased.		Unaltered.		Increased.		Decreased.		Unaltered.		Increased.		Decreased.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
6	47	50.0	47	50.0	93	69.4	36	26.9	5	3.7	16	69.6	7	30.4		
12	420	75.5	136	24.5	251	70.3	35	9.8	71	19.9	17	65.4	8	30.8	1	3.8
18	103	65.2	55	34.8	108	74.5	18	12.3	19	13.1	11	57.9	3	15.8	5	26.3
24	135	76.7	41	23.3	106	79.7	8	6.0	19	14.3	9	60.0	3	20.0	3	20.0
30	205	75.1	68	24.9	140	73.7	30	15.8	20	10.5	4	66.7	0	....	2	33.3

TABLE II.—RECORD OF PUPILS TAKING PROPHYLACTIC TREATMENT.

Time under observation, mos.	Normal.				Slightly enlarged.						Moderately enlarged.					
	Unaltered.		Increased.		Unaltered.		Increased.		Decreased.		Unaltered.		Increased.		Decreased.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
6	17	94.4	1	5.6	54	69.2	1	1.3	23	29.5	9	81.8		...	2	18.2
12	344	99.7	1	0.3	187	45.5		...	224	54.5	10	23.8		...	32	76.2
18	73	100.0		...	72	52.3	1	0.7	64	46.7	7	28.0		...	18	72.0
24	184	100.0		...	72	37.9	1	0.5	117	61.6	2	7.7		...	24	92.3
30	288	100.0		...	92	28.5		...	231	71.5	1	2.6		...	38	97.4

TABLE III.—SUMMARY OF RECORDS OF PUPILS TAKING AND NOT TAKING PROPHYLACTIC TREATMENT.

	Taking.		Not taking.	
	Totals.	Per cent.	Totals.	Per cent.
Normal:				
Unchanged	906	99.8	910	72.4
Increased	2	0.2	347	27.6
Slightly enlarged:				
Unchanged	477	41.9	698	72.8
Increased	3	0.3	127	13.3
Decreased	659	57.8	134	13.9
Moderately enlarged:				
Unchanged	29	20.3	57	64.0
Increased	...	....	21	23.6
Decreased	114	79.7	11	12.4
Total	2190	..	2305	

Prevention. The preventive value of the treatment is shown in the column marked "unchanged" and "increased." Taking the totals for the periods of six months each the following results were obtained. Of those that were normal at the first examination and did not take iodin, 347, or 27.6 per cent, had enlarged thyroids, while of those that were normal at the first examination and took iodin as outlined, 2, or 0.2 per cent, had enlarged thyroids. These two instances of enlargement were investigated.

The first pupil, aged sixteen years, had her thyroid examined and classified as normal on May 2, 1917, October 17, 1918, and December 3, 1918. At the examination on October 15, 1919, it was classified as slightly enlarged. This girl had taken 2 gm. of sodium iodide during each of the five possible periods, May, 1917, November, 1917, May, 1918, December, 1918 and May, 1919. A special examination was made on January 13, 1920, when the enlargement of the thyroid was verified. That this enlargement was acquired rather than congenital was shown by the absence of a pyramidal process of the thyroglossal tract. The tonsils were markedly enlarged and abnormally hyperemic. On direct questioning we were informed that the pupil was subject to recurrent attacks of tonsillitis. There was also slight enlargement of the lymphoid tissue at the base of the tongue and in the nasopharynx, and the general impression was that of a neurotic individual with general lymphoid hyperplasia.

The second girl, aged fifteen years, had her thyroid first examined and classified as normal on November 27, 1918. At the examination on October 16, 1919, it was classified as slightly enlarged. This girl had taken 2 gm. sodium iodide during each of the two available periods, November, 1918, and May, 1919. A special examination was made January 13, 1920, when the thyroid enlargement was verified. Careful inspection revealed the presence of Hutchinson teeth, depressed nasal arch and interstitial keratitis. We considered the case as one of neglected congenital syphilis.

Of the cases classed as having slightly enlarged thyroids at the first examination and *not taking* the prescribed iodin, 127, or 13.3 per cent, underwent further enlargement, while among those *taking* the prescribed treatment only 3, or 0.3 per cent, underwent further enlargement. Two of these 3 were reëxamined on January 13, 1920, and the previous finding verified. One of these was another case of chronic infection of the tonsils with recurrent attacks of tonsillitis during the last year. In the second girl superficial inspection failed to show any pathologic condition to account for the enlargement. The third girl was not present for examination. These 5 cases were the only instances that showed enlargement of the thyroid out of 2190 pupils. Of the 2305 cases *not taking* iodin, 495 showed thyroid enlargement. Of the group with small goiters *taking* iodin, 659, or 57.8 per cent, returned to normal, while of the same group *not taking* iodin *at school*, 134, or 13.9 per cent,

returned to normal. However, we know that there is an error in the last figure, for many cases not taking iodin under the school jurisdiction were taking it in some form from their physician. No attempt has been made to detect or estimate this error.

In the practical application of the preventive treatment one must keep in mind the three periods when simple thyroid enlargements most commonly occur, namely, (*a*) fetal period; (*b*) adolescence; (*c*) pregnancy.

(*a*) The prevention of goiter in the mother and the fetus is as simple as the prevention of goiter which develops during adolescence. Practically it would seem that the prevention of goiter during these periods, *i. e.*, (*a*) and (*c*) is properly the responsibility of individual members of the medical profession supplemented by education of the public.

(*b*) The prevention of goiter in the adolescent period, on the other hand, should be a public health measure under state, county or municipal control. The existing systems of organization of the schools, both public and private, are sufficient to handle all the details without additional aid or expense. Education of the pupils could be combined with the actual administration of iodin, so that after leaving school they could continue the treatment if necessary. In industrial medicine physicians could render an important service in this direction. As thyroid enlargement is approximately six times as frequent in girls as in boys, each community must decide whether it will include both sexes in prophylactic measures, as it must also decide regarding the ages when the use of iodin should begin and end. In this climate probably the maximum of prevention, coupled with the minimum of effort, would be obtained by the administration of iodin between the ages of eleven and seventeen years. As applied to our schools this would mean beginning with the fifth grade.

Method and Form of Administration. As has been shown, iodin is taken up by the thyroid gland when given by mouth, by inhalation or by external application. And it makes very little difference from a scientific point of view what form of iodin is used; the thyroid gland will take up iodin from the most stable compound, *i. e.*, mercuric iodide. Weith reports favorable therapeutic results from the inhalation of iodin secured by the suspension in the school room of a wide-mouthed bottle containing 10 per cent tincture of iodin.

It has been suggested by Sloan that in these mildly goitrous districts a mixture of small amounts of sodium iodide in common table salt could be made which would suffice for all iodin therapy. However, we feel that the most satisfactory method is the individual oral administration of definite small amounts of some salt of iodin, either in solution or tablet form. For private use the well-known U. S. P. preparations, syrup of ferrous iodide and syrup of hydriodic

acid, are excellent. As described above, as a public health measure, we use 2 gm. of sodium iodide over a period of two weeks and repeated twice yearly. This dosage has prevented enlargement of the thyroid in more than 99 per cent of the children in this mildly goitrous district.

When one recalls the small amount of iodin required to saturate the normal thyroid and the specific affinity of this gland for iodin it is perfectly obvious that only very small amounts are needed. The normal thyroid contains about 5 mgm. of iodin per gram of dried gland; 25 to 30 mgm. is the total storage capacity. From this it is clear that a few milligrams of iodin daily over a longer period (a month or more) would produce optimum thyroid effects.

The prevention of thyroid enlargement in individuals with other diseases or in those residing in extremely goitrous districts as in some glacial valleys of Alaska and British Columbia, and in certain districts of the Alps and Himalayas, might require larger amounts of iodin than in normal individuals indicated above.

Possible Ill Effects. As was stated above there was some anxiety among medical men as to the possible ill effects of giving iodin promiscuously. Some men anticipated many cases of exophthalmic goiter while others looked for an outbreak of iodide rash. The actual results were better than we had hoped for. In all the cases taking the prescribed 2 gm. of sodium iodide twice yearly there was not a single instance of exophthalmic goiter nor any evidence of a nervous irritability simulating it. In all there were 11 cases of iodide rash, and 6 of these cases were so mild that the girls did not even stop the treatment; 5 cases, however, caused sufficient difficulty for the treatment to be stopped when the rash cleared up promptly.

Both of these possibilities were considered and mentioned in each school. In all there were over 3000 different girls taking the prophylactic treatment, many of whom took it for three years, and among these the sum total of the ill effects was a mild rash in less than 0.4 of 1 per cent.

The Possibility of the Elimination of Endemic Goiter throughout the World. Following the publication of the results of our first year's work in Akron the public schools of Kent and Ravenna adopted the same procedure, and in 1919 the village of Berea began the prevention of goiter through the schools on the same plan. In the spring of 1920 we completed a survey of goiter among the school children of Warren, Ohio, including all boys and girls from the fifth to the twelfth grades inclusive. As the incidence of thyroid enlargement was low—24.4 per cent in girls and 9.5 per cent in boys— we advised the school physician and nurse that we considered it sufficient in this vicinity to provide each school with a stock solution of sodium iodide and treat each goiter as soon as it was detected. This method has been in operation in Warren for one year, and is just now being started in Niles. This same method of treatment is

being practised in some of the large factories of Cleveland where many young women are employed, and it is being provided in the different factories of the National Lamp Works in eight different cities of the United States.

It is interesting to note that in the spring of 1918 Prof. R. Klinger, of Zurich, Switzerland, undertook to carry out the same treatment in the schools there. This was soon started with a different method of administration, but practically the same amounts of iodin as we used in Akron. In January, 1921, Klinger published the results of the first sixteen months' treatment, reporting extraordinary results, even though he was working in some schools in which the children were 100 per cent goitrous. Klinger's results certainly supply striking confirmation of the results we obtained in Akron. It is even more gratifying to know that recently this same plan of the prevention of goiter has been recommended to the goiter commission of Switzerland, to be carried out as a public health measure throughout the whole state, the most noted endemic goiter nation in the world.

The same imagination which developed the practical application of the principle of the prevention of goiter can now see, a few generations hence, the closing of the chapters on endemic goiter and cretinism in every civilized nation in the world.

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THE OCCURRENCE OF PHYSICAL SIGNS SUGGESTIVE OF AORTIC DEFECTS.[1]

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A HEALTH survey of the police and firemen of the city of Philadelphia was recently conducted by the Henry Phipps Institute

[1] Read before the Thirty-eighth Annual Meeting of the American Climatological and Clinical Association, Lenox, Mass., June, 1921.

of the University of Pennsylvania, having for its objects (1) the determination of the incidence of physical defects which might reduce the efficiency of or seriously interfere with the working capacity of the individual; (2) the obtaining of information upon the value of a general health survey in the detection of disease; and (3) the securing of data in regard to the best method for conducting such an examination, the time required, cost, etc. The information was desired as the Institute was planning the establishment of a department to provide general health examinations for industrial plants in and about the city of Philadelphia.

Every member of the police and fire departments was given a complete general physical examination, including a study of the height, weight, temperature, pulse, eyes, ears, nose, throat, teeth, skin, genitalia, inguinal rings, deformities and defects, blood-pressure, heart, lungs, etc. The routine examinations were performed by Drs. John S. Scouller, H. F. Keating and William R. Gilmour under the direction of the writer of this article acting as physician-in-charge. During the examination all men who were found to be normal or whose defects were only slight were dismissed, but all those in which serious defects were detected or suspected were referred to the physician-in-charge for reëxamination, who arranged for special examinations, such as Wassermann tests, roentgen-ray examinations, electrocardiographic studies, etc., either directly or in coöperation with Dr. Hubley R. Owen, chief surgeon of the police and fire departments. The blood-pressure was taken routinely in every individual and the urine examined in every case in which the systolic pressure was 150 mm. of mercury or over, or in which the examination of the urine was indicated.

After only a small proportion of the 5706 men had passed through our hands it was found that there was a relatively large number in which the diagnostic interest was mainly centered in the aortic region. An effort was made to study these cases in detail, as far as our facilities permitted, the results forming the basis of the present paper. Special attention was given this group for the reason that it is composed of men which impressed one as being "poor risks," especially when occurring in the firemen, whose work is distinctly more strenuous than that of the policemen.

The cases under consideration were encountered under conditions which did not permit of clinical study over a long period of time, and in no case was the history of previous disease or symptomatology obtained, the cases being considered entirely on the basis of physical evidence of disease. It is, therefore, evident that we must confine ourselves to a consideration of what physical signs may be considered as definitely indicating the presumptive presence of dilatation of the aorta and what correlated evidence should be sought in an effort to discover the etiologic factor in the individual case.

Physical Signs. A description of the physical signs upon which a positive diagnosis of aortic disease may be based is an exceedingly difficult one, as the writers upon this subject are not in complete accord and frequently are not as clear as one would desire. This is due to the fact that their descriptions are usually confined to special diseases while the physical signs vary with the pathologic changes in the aorta.

It is not my purpose or desire to enter into a discussion of the various manifestations of arterial disease but to confine myself to a consideration of the abnormal physical signs which may be encountered in the routine examination of a large number of men, signs which suggest pathologic changes in the aorta.

The signs which have been attributed to elongation, dilatation, sclerosis or inflammation of the aorta are briefly as follows: Dulness over the manubrium, extending to the right in the 2d and 3d interspace, with or without localized pulsation recognizable by inspection or palpation.

Accentuation of the aortic second sound which may often be clanging in character or possess a tympanic quality and may frequently be accompanied by a palpable diastolic shock.

A systolic murmur may be present at the aortic cartilage which occasionally may be transmitted to the vessels of the neck and may at times be accompanied by a systolic thrill.

Others signs which have been noted are: Visible pulsation in the peripheral arteries, displacement of the right subclavian upward to a position above the clavicle, suprasternal pulsation, abnormal mobility of the apex-beat with change of position, pericardial friction rub and other signs associated with mediastinal inflammation or peri-aortitis.

The signs which have been considered of most value are manubrial dulness and alteration in tone of the second aortic sound, the latter being considered of the greatest value in recognizing aortitis in its earlier stages.

During our examination of the police and firemen we encountered 49 cases which presented evidence suggesting the presence of aortic changes. One of these, a man aged thirty-six years, with a definite specific history, showed signs definitely pointing to the presence of an aneurysm, the diagnosis being confirmed by roentgen-ray examination. This we have omitted from our series, leaving 48 cases for consideration. It will be noted that in many of the cases the records are incomplete, certain of the physical signs having apparently been omitted or not recorded. This is due to the fact that at certain periods during the examination time did not permit of as thorough an examination as one would desire or else in the rush of work the findings were not completely recorded. Failure to report for special laboratory studies, such as Wasser-

mann tests, roentgen-ray and urine examinations, largely accounts for the omissions in laboratory reports.

While these omissions may detract from the scientific value of the observations in this study, they in no way affect the primary object of this paper, which is to call attention to the relative frequency (at least in the group studied) with which physical signs may be encountered strongly suggestive of pathologic changes in the aorta. A very important feature was the almost total absence of any suspicion on the part of the individual that he was not in good health.

For convenience in presenting the cases we have arranged them in groups according to the skiagraphic findings as follows:

		Cases
Group I.	Roentgen-ray shows definite aortic changes	9
Group IIa.	Roentgen-ray shows slight aortic changes	8
Group IIb.	Roentgen-ray shows questionable aortic changes	3
Group III.	Roentgen-ray shows absence of aortic changes	13
Group IV.	No roentgen-ray examination made	15

The roentgen-ray studies were made by Dr. Alfred S. Doyle, assistant to Dr. H. K. Pancoast, roentgenologist to the University Hospital.

Tables have been prepared showing each case studied, the more important physical signs observed and such correlated clinical data as might be of interest.

The first 7 men in this group, all over forty-seven years of age, showed a definite dilatation of the aorta. A study of the physical signs recorded in these cases would indicate that the character of the second aortic sound, with a systolic aortic murmur or manubrial dulness, was the most characteristic sign of the dilatation. The 2 cases without accentuation of the aortic second were ones in which the blood-pressure was normal. (See Table I.)

It must be borne in mind that the record of "accentuation of the second aortic sound" refers merely to accentuation and not to the quality of the second sound itself. These 48 cases were considered as possible cases of aortic disease on account of the fact that they presented signs which we considered indicative of aortic disease, the sign which we laid most stress upon being the clanging quality of the aortic second sound. The record of "accentuation of the aortic second sound" must not be taken to represent this change in the quality of the sound.

Of the two remaining cases one showed no dilatation but marked expansible pulsation by the fluoroscopic examination, with a systolic aortic murmur in a case of aortic regurgitation, and one showed an abnormal pulsation below the left clavicle due to a tortuous aortic arch, especially marked at this point.

GROUP I.—DILATATION OF AORTA WITH X-RAY EXAMINATION.

Case No.	Age.	Accentuated aortic second sound.	Aortic systolic murmur.	Dulness over manubrium.	Wassermann test.			Urine examination.					Blood-pressure.			Associated cardiac defects, physical signs and symptoms.	Report of Roentgen-ray examination of aorta and lungs.
					Positive.	Negative.	Omitted.	Normal.	Specific gravity.	Albumin.	Sugar.	Omitted.	Systolic.	Diastolic.	Pulse pressure.		
1884	52	++	+	−	..	..	+	..	1006	Tr.	0	..	170	90	80	Aortic regurg.?	First portion of arch broad and pulsating; mod. dilatation of entire arch, especially the ascending portion.
3945[1]	53	+	+	−	..	..	+	..	1012	Pres.	0	..	205	140	65	Extrasystoles	Decided widening of aorta; no unusual pulsation.
3207	48	+	+	−	+	..	..	+	−	..	..	..	140	80	60	Mitral insuf.	Widening of arch and marked pulsation.
3939	60	+	+	−	..	+	..	..	1012	Tr.	+	..	185	110	75	Mitral insuf.?	Marked dilatation of arch and considerable pulsation; almost aneurysmal.
2133	50	++	0	+	..	+	..	..	1024	Ft. tr.	0	..	205	125	80	Pain over sternum	Considerable enlargement of transverse and descending portions of arch.
3725	50	0	+	−	..	+	..	+	−	..	..	..	125	70	55	Mitral insuf.? and aortic regurg.?	Increase in size of first portion of arch and fairly marked expansile pulsation; slight dilatation ascending arch (old tb.?).
3823[2]	68	0	+	−	..	..	+	..	..	..	..	+	130	80	50	Aortic regurg. and rel. mitral insuf.?	Widening of first portion of arch in both directions (old pulm. tubere.?).
5085	41	0	+	−	..	..	+	+	1021	..	..	..	155	80	75	Aortic regurg.	Arch not dilated but marked expansile pulsation (pulm. fibrosis).
2895	41	0	0	−	..	..	+	..	..	..	..	+	120	80	40	Pulsation below left clavicle, out to mid-clavic. line	Tortuous aortic arch, especially in second left interspace.

[1] Died suddenly since examination.
[2] Has resigned (on account of ill health?) since examination.

GROUP II A.— SLIGHT DILATATION OF AORTA WITH X-RAY EXAMINATION.

Case No.	Age.	Accentuated aortic second sound.	Aortic systolic murmur.	Dulness over manubrium.	Wassermann test.			Urine examination.					Blood-pressure.			Associated cardiac defects, physical signs and symptoms.	Report of Roentgen-ray examination of aorta and lungs.
					Positive.	Negative.	Omitted.	Normal.	Specific gravity.	Albumin.	Sugar.	Omitted.	Systolic.	Diastolic.	Pulse pressure.		
58	41	+	+	−	..	+	..	..	..	..	..	+	145	90	55	Prominent superficial veins over chest	First portion of arch a little widened in both directions.
3922	57	+	+	−	..	+	..	..	1006	Ft. tr.	0	..	140	80	60	Extrasystoles; auric. fibrill.?	Slight dilatation of ascending arch.
22	35	++	0	+	..	+	..	..	....	..	..	+	130	95	35	....	Slight dilatation of ascending arch.
5325	57	+	0	+	..	..	+	..	1020	Ft. tr.	0	..	180	110	70	Cardiac dilatation	Ascending arch slightly widened in oblique position.
3893	66	0	+	−	..	+	..	..	−	Cl.	0	..	155	95	60	Rel. mitr. insuf.; auric. fibrill. (electrocard.)	First portion of arch slightly increased in width.
2157	51	0	+	−	..	+	..	+	−	..	..	..	155	90	65	Aortic and mitral regurg.	Aorta slightly tortuous and slightly dilated in ascending portion; no aneurysm.
3744	54	0	+	−	..	+	..	+	1010	..	..	..	125	85	40	Rel. mitral insuf.	Slight increase in width of first portion of arch in both directions; pulsation not marked.
2068	40	0	0	−	..	..	+	..	..	..	..	+	145	80	65	Mitral regurg.?; heart irreg.; visible pulsation in vessels.	Arch of aorta slightly increased in width.

GROUP II B.—QUESTIONABLE DILATATION OF AORTA WITH X-RAY EXAMINATION.

Case No.	Age.	Accentuated aortic second sound.	Aortic systolic murmur.	Dulness over manubrium.	Wassermann test.			Urine examination.					Blood-pressure.			Associated cardiac defects, physical signs and symptoms.	Report of Roentgen-ray examination of aorta and lungs.
					Positive.	Negative.	Omitted.	Normal.	Specific gravity.	Albumin.	Sugar.	Omitted.	Systolic.	Diastolic.	Pulse pressure.		
3281	53	+	+	−	..	+	..	..	1036	Tr.	+	..	195	95	100	Mitral insuf.	Arch possibly slightly increased in oblique view.
2890	53	0	+	−	..	+	..	+	−	..	..	..	125	80	45	Mitral regurg.?	Slight widening of ascending arch in ant.-post. and oblique views, but not unusual for age.
2264	44	+	+	+	..	+	..	..	..	..	..	+	135	80	55	.....	Good pulsation of ascending arch which is possibly slightly broadened but not to an unusual degree.

GROUP III.—AORTIC CHANGES SUSPECTED CLINICALLY, WITH NEGATIVE X-RAY FINDINGS.

Case No.	Age.	Accentuated aortic second sound.	Aortic systolic murmur.	Dulness over manubrium.	Wassermann test.			Urine examination.					Blood-pressure.			Associated cardiac defects, physical signs and symptoms.	Report of Roentgen-ray examination of aorta and lungs
					Positive.	Negative.	Omitted.	Normal.	Specific gravity.	Albumin.	Sugar.	Omitted.	Systolic.	Diastolic.	Pulse pressure.		
365	42	+	+	+	..	+	..	+	1005	..	..	..	155	75	80	Rel. mitral insuf.	Negative.
439	35	+	+	+	..	+	..	..	..	..	..	+	155	90	65	Rel. mitral insuf.	Negative.
724	53	+	+	+	..	..	+	..	..	..	..	+	170	85	85	.....	Negative.
2820	36	+	+	−	..	..	+	..	..	..	..	+	125	75	50	Mitral regurg.	Negative.
4627	62	+	+	+	..	..	+	..	1020	Tr.	0	..	160	70	90	Aortic regurg.	Aorta not enlarged to any unusual extent.
189	43	0	0	+	..	+	..	..	..	..	..	+	130	85	45	.....	Negative.
485	29	+	0	0	+	..	..	+	1015	..	..	..	185	100	85	.....	Negative.
1806	37	0	+	+	..	+	..	..	..	..	..	+	125	85	40	.....	Negative.
4530	22	−	+	+	..	+	..	..	1007	V. ft. tr.	0	..	165	85	80	Soft double aortic and systolic murmur at apex; reëxam. neg.	Negative.
5397	46	0	+	0	..	..	+	..	..	..	..	+	130	80	50	.....	Negative.
2272	52	0	+	−	..	..	+	+	1025	..	..	..	155	95	60	.....	Negative.
2900	65	0	+	−	..	+	..	..	1022	V. ft. tr.	+	..	155	100	55	Rel. mitral insuf.; chronic myocarditis	Negative.
1934	52	0	0	+	+	..	..	..	1017	V. ft. tr.	0	..	140	85	55	.....	Negative.

GROUP IV.—AORTIC CHANGES SUSPECTED CLINICALLY, NO X-RAY EXAMINATION MADE.

Case No.	Age.	Accentuated aortic second sound	Aortic systolic murmur.	Dulness over manubrium.	Wassermann test.			Urine examination.					Blood-pressure.			Associated cardiac and pulmonary defects and physical signs.
					Positive.	Negative.	Omitted.	Normal.	Specific gravity.	Albumin.	Sugar.	Omitted.	Systolic.	Diastolic.	Pulse pressure.	
4649	63	++	0	++	..	..	+	+	1023	..	..	..	165	105	60	Myocarditis; auric. fibrill.?
1112	64	++	+	−	..	..	+	+	1010	..	..	..	185	30	155	Rel. mitral insuf.?
4526	26	+	+	−	+	..	..	..	1021	Cl.	0	..	175	85	90	Mitral regurg.?
5549	50	+	+	−	..	..	+	..	1020	V. ft. tr.	0	..	190	120	70	Mitral regurg.
471	29	+	0	+	..	+	..	+	1002	..	..	..	180	90	90	
1801[1]	52	+	0	+	..	..	+	..	..	..	..	+	155	85	70	
4554	37	+	0	−	..	..	+	..	1020	V. ft. tr.	0	..	160	100	60	Cardiac hypertrophy; overacting heart.
4393	38	0	+	+	..	..	+	..	1007	V. ft. tr.	0	..	155	75	80	Visible pulsation in vessels.
4328	41	0	+	−	..	..	+	..	..	..	..	+	115	80	35	Mitral regurg.?
5103	50	0	+	−	..	..	+	..	1027	Cl.	0	..	165	105	60	Extrasystoles; aortic regurg.
841	49	0	+	−	..	..	+	..	..	..	..	+	140	65	75	Mitral sten. and regurg.; mitral regurg.
2939	60	0	+	−	..	..	+	+	1016	..	..	..	165	90	75	Emphysema.
2356	59	0	+	−	..	..	+	..	..	..	..	+	130	75	55	Mitral regurg.
3236	60	0	+	−	..	+	..	..	1020	V. ft. tr.	0	..	150	80	70	Mitral regurg.; aortic and mitral regurg.; auric. fibrill.?
3435	44	0	+	−	..	..	+	..	..	..	..	+	130	50	80	Marked suprasternal pulsation.

[1] Died since examination (of uremia?).

This group consisted of 8 cases in which the roentgen-ray revealed slight increase in width of a portion of the aorta, and yet the various physical signs occurred with about the same relative frequency as in Group I. It will be noted that in this group the systolic blood-pressure was, as a rule, lower than in Group I, an average of 147 compared to 159. (See Table II*a*).

Here the signs also occurred with fair constancy even in three cases with questionable roentgen-ray findings. (See Table II*b*.)

This group consists of 13 men in which the roentgen-ray examination was negative, but in all of which definite physical signs were noted pointing to aortic changes. In two cases (485 and 1934) a positive Wassermann test was obtained and may be considered as cases of specific aortitis without dilatation or marked elongation of the aortic arch.

In 5 cases the Wassermann test was not made so that they may be considered as possible cases of aortitis. There were, however, 6 cases in which the Wassermann test was negative and which showed definite physical signs of aortic change with negative roentgen-ray findings. In these cases it is difficult to explain the apparent discrepancy between the physical findings and the roentgen-ray study. In 1 case there was a slight albuminuria with hypertension in a young man aged twenty-two; in 2 other cases the systolic blood-pressure was rather high for the age and in 2 the pressure was normal. (See Table III.)

There were 15 cases in which no roentgen-ray examination was made and with 3 exceptions no Wassermann test. These were nearly all cases presenting evidence of cardiac disease in addition to the suspected aortic change, many of them also showing albuminuria. (See Table IV.)

Summary. In the examination of large bodies of men more attention should be directed to the study of the upper anterior chest than is usually devoted to this region, especially, but by no means exclusively, in those over forty years of age. In the present study of 5706 men with an average age of forty-five to forty-nine years, signs were found suggesting changes in the aorta in about 0.85 per cent. The literature on this subject is surprisingly scanty when one considers the importance of the condition. The statement has been made by Clifford Allbutt[2] that "Chronic disease of the ascending aorta without aneurysm is far more common in middle life, in early adult life and even in youthful life than we are wont to realize, and is for the most part insidious." An observation which the present study would appear to confirm.

The nature of our study was of such a character that it is impossible to arrive at any very definite conclusions as regards to etiology; 5 showed a positive Wassermann reaction (including

[2] Diseases of the Arteries, including Angina Pectoris, 1915, **2**, 190.

the case of aneurism), in 20 it was negative and in the remaining 24 it was not taken. In only 3 instances was sclerosis of the peripheral arteries (radials) noted among the 44 cases in which a positive Wassermann test was not present or not made, although the absence of sclerosis in the peripheral vessels does not exclude the possibility of aortic change. In an effort to show the type of case in which this condition was noted we have prepared the following table:

TABLE SHOWING ASSOCIATED DEFECTS (CASES WITH POSITIVE WASSERMANN TESTS BEING ELIMINATED.)

	Wassermann test negative.		Wassermann test not made.		Total.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Hypertension:						
Cardiorenal	7	35.0	2	8.3	9	20.4
Cardiac	3	15.0	4	16.6	7	15.9
Renal	1	5.0	6	25.0	7	15.9
Alone	1	5.0	2	8.3	3	6.8
Slight—urine not examined	0	0	2	8.3	2	4.5
Cardiac	0	0	5	20.8	5	11.3
Questionable	3	15.0	1	4.1	4	9.0
None—urine not examined	5	25.0	2	8.3	7	15.9
Total	20	100.0	24	99.7	44	99.7

It will be noted that the large proportion of cases were associated with some degree of hypertension, in 60 per cent of those with negative Wassermann test and in 64.5 per cent of those in which no Wassermann test was made. This corresponds with the observations of Smith and Kilgore,[3] who found frequent dilatation of the arch in their roentgen-ray study in individuals under the age of fifty years in non-syphilitic conditions, especially in chronic nephritis with hypertension.

In conclusion, we would state that in the examination of a large number of men, non-syphilitic cases are encountered with relative frequency in which the physical signs strongly suggest the presence of aortic changes, which may or may not be appreciable by roentgen-ray examination.

[3] AM. JOUR. MED. SC., April, 1915.

THE HEART MUSCLE CHANGES IN PNEUMONIA, WITH REMARKS ON DIGITALIS THERAPY.*

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The recent article by Brooks and Carroll[1] upon the management of the heart in pneumonia, with reference to digitalis therapy, has stimulated an analysis of personal records of patients under the care of officers in the Medical Service of the U. S. Army Base Hospital, Fort Riley, Kansas (Camp Funston), from October 18, 1917, to December 31, 1918. Brooks and Carroll based their deductions upon an analysis of 5000 protocols of patients who died from pneumonia in the A. E. F. (Dijon). Their study consisted largely of instances of influenza pneumonia. The present series will deal with 1205 lobar and bronchopneumonia patients, including 259 autopsies. A series of 2657 patients with influenza pneumonia[2] treated during the interval September 15 to November 1, 1918, has been excluded from the statistics since but a relatively small number of autopsies were performed and since, because of the large number treated in a short period it was impossible to draw deductions as to the efficiency of the digitalis treatment employed.

The Cause of Death. Such a large proportion of pneumonia deaths have appeared to have resulted from circulatory failure that interest, from the standpoint of treatment, has largely centered upon the condition of the heart. Those of large experience in the pathology of the disease have realized that in many cases acute parenchymatous degenerative changes were commonly found to be present in many organs aside from the heart muscle. It has by no means been decided that the degenerative changes, in the degree commonly found, have been responsible for the usual death in this disease, although it may be granted that the function of the various organs, such as the liver, kidney and spleen, may have been more or less seriously disturbed. When the marked recuperative powers of the liver and kidneys are recalled in poisoning from chloroform, arsenic and other toxic agents, as well as the ability of the heart muscle to restore its normal function after prolonged serious illness, such as typhoid and diphtheria, in which degenerative changes must have occurred, the question may be raised whether in an acute pneumonia without sepsis death has resulted from the disturbed function of these organs brought about, *per se*, by the degeneration

* Read before the American Climatological and Clinical Association, Lenox, Mass., June 4, 1921. Published by authority Surgeon-General U. S. Army.

[1] Am. Jour. Med. Sc., December, 1920, **160**, 815.

[2] Swift, George W., and Stone, Willard J.: Jour. Am. Med. Assn., February, 1919, **72**, 487.

found to be present. That these processes have operated to disturb function may be conceded. But that they have exerted the essential influence leading to death may be questioned in many instances. It may be believed that the matter will resolve itself into a question of extent and degree rather than kind.

Those who have witnessed any large series of pneumonia autopsies must have been impressed with the extensiveness of the septic changes such as empyema, pericarditis, substernal pus pockets, lung abscess, subdiaphragmatic abscess and peritonitis present, in one form or another, in a considerable proportion of the cases. For example, in Table I it will be noted that in 1205 cases sepsis in one form or another was present clinically, or at autopsy, in 283, or 23.5 per cent. Report has previously been made[3] of the occurrence of acute and subacute purulent pericarditis which was present in 58, or 19.3 per cent, of 300 pneumonia autopsies of all types, including influenza pneumonia. Of itself sepsis has appeared to be the most important cause of death in the subacute or chronic forms of the disease, that is, in those who have died after the fourteenth day of illness.

TABLE I.

	Total cases.	Sepsis.	Per cent.
Oct. 18, 1917, to Jan. 15, 1918 . . .	279	66	23.6
Jan. 16, 1918, to May 18, 1918 . . .	592	134	22.6
June 1, 1918, to Dec. 31, 1918 . . .	334	83	24.8
Total	1205	283	23.5

In our experience the septic infection appeared to have spread, in most instances, by way of the lymphatics rather than by the blood stream. In a large proportion the blood cultures were sterile and we were impressed by the comparative rarity of such complications as endocarditis, septic infarction of the kidneys or the spleen and meningitis and phlebitis, which may have been regarded as evidences of blood-stream transportation.

In the consideration of those causes other than sepsis responsible for death in many acute forms of the disease, failure of the cardiac muscle to meet the demands made upon it has appeared as a prominent factor. In few other acute diseases have adverse conditions conspired to defeat the purpose of function on the part of the heart as in pneumonia. The mechanical features of obstruction to the pulmonary circuit offered by the consolidation with its consequent right heart strain, the anoxemia, toxemia and blood concentration, have all directly or indirectly operated to disturb function.

The Heart Muscle Changes. The protocols of 259 autopsies upon pneumonia patients in which the condition of the heart muscle was described have been analyzed. The heart-muscle changes

[3] Stone, Willard J.: Jour. Am. Med. Assn., July 26, 1919, **254**, 73.

have been shown in Table II. It should be stated that particular interest as to the condition of the heart muscle on the part of the pathologists (Dr. Henry W. Cattell, Dr. F. K. Bartlett, Dr. S. T. Nicholson, Jr., and Dr. Arthur A. Smith, former officers in the Medical Corps, U. S. Army) was solicited because of the fact that large doses of a standardized tincture of digitalis were routinely used in the treatment of the disease.

TABLE II.

Gross changes.	Lobar pneumonia (89 autopsies), per cent.	Broncho-pneumonia[4] (112 autopsies), per cent.	Sepsis following pneumonia (58 autopsies), per cent.
Heart muscle normal	57.3	66.1	37.9
Heart muscle degeneration	42.4	33.9	62.1
Right ventricle dilatation	39.4	36.6	20.8
Left ventricle dilatation	12.4	10.0	12.1

It will be noted that in 89 lobar pneumonia autopsies dilatation of the right ventricle was found in 39.4 per cent, while in 112 bronchopneumonia autopsies, which included interstitial and confluent lobular types, dilatation of the right ventricle was found to be present in 36.6 per cent. The left ventricle was found to be dilated in 12.4 per cent of the lobar pneumonia and in 10 per cent of the bronchopneumonia autopsies. In 58 autopsies upon patients who died as a result of sepsis following pneumonia the right ventricle was found to be dilated in 20.8 per cent. A majority of these patients had recovered from their acute pneumonia.

These figures are higher than those reported by Berry[5] in his analysis of 400 pneumonia autopsies performed at the Boston City Hospital. He found that cardiac dilatation was reported by the pathologists but 6 times in the 400 cases. It would be interesting to know what criteria served to establish the diagnosis of dilatation, or the absence of it, on the part of the various pathologists who performed the autopsies over the period of years mentioned in the report, for it is difficult to believe that dilatation only occurred in less than 1 per cent of the cases.

In the present series the gross appearance of the heart muscle was described as normal in 57.3 per cent of the 89 lobar pneumonia autopsies while degenerative changes were believed to be present in 42.7 per cent. In the 112 autopsies upon bronchopneumonia patients (including the interstitial and confluent lobular types) the gross appearance of the heart muscle was described as normal in 66.1 per cent, while degenerative changes were noted in 33.9 per cent. Brooks and Carroll in the Dijon study have reported that an inflammation or degeneration of the heart muscle was present

[4] Under the term bronchopneumonia have been included confluent lobular and interstitial types.

[5] Medical Clinics of North America, September, 1920, **4**, 571.

in 748 of 1651 protocols, or 45.3 per cent. As would be expected in the 58 autopsies upon patients who died with sepsis following pneumonia (such as empyema, purulent pericarditis, multiple lung abscesses, substernal pus pockets, subdiaphragmatic abscess, peritonitis or meningitis) evidences of heart-muscle degeneration were present in a larger number, 62.1 per cent.

The Microscopical Findings. The sections of heart muscle from 34 autopsies upon lobar pneumonia patients and from 37 autopsies upon bronchopneumonia patients (including the confluent lobular and interstitial types) have been studied. The specimens were prepared under the direction of Dr. O. F. Broman, formerly chief of the laboratory service in the hospital. The findings have been presented in Table III.

TABLE III.—MICROSCOPICAL FINDINGS.

	Lobar pneumonia (34 autopsies), per cent.	Broncho-pneumonia[6] (37 autopsies), per cent.
Heart muscle normal	20.6	40.5
Parenchymatous degeneration	52.9	37.8
Fatty degeneration	11.7	8.1
Leukocytic and round-cell infiltration	8.9	10.8
Hyaline degeneration	2.9	
Interstitial myocarditis	2.9	2.7

Parenchymatous degeneration (cloudy swelling) was present in 52.9 per cent of the sections in lobar pneumonia and in 37.8 per cent of the sections in bronchopneumonia. As will be noted in the table other degenerative changes were more marked in the lobar pneumonia than in the bronchopneumonia sections. Fragmentation of the muscle fibers was not described as a condition necessarily of pathological importance, even though extensive in some of the sections, because of its occurrence in many apparently normal specimens.

Digitalis Therapy in Pneumonia. Beginning January 15, 1918, all patients with pneumonia received during the first twenty-four to thirty-six hours after admission to the hospital their total dosage, according to estimated body weight, of a special tincture of digitalis prepared in the hospital by Sergeant Moody, in charge of the pharmacy. The tincture was standardized by the cat method of Hatcher[7] through the kindness of Dr. Cary Eggleston, of Cornell Medical School. The tincture was prepared from Allen's English leaves as follows: The entire contents of the one-pound cans were finely ground and percolated with 75 per cent alcohol. Since the cans were hermetically sealed and moisture and molds have been known to cause deterioration in the leaves after the cans were opened

[6] Including confluent lobular and interstitial types.
[7] Am. Jour. Pharm., 1910, **82**, 360.

the tincture was made up in large quantity, using the entire contents of the cans and avoiding cans opened for previous batches which may have contained small quantities of left-over leaves. Many batches of tincture so prepared preserved their potency for a year when kept under conditions of ordinary care. The tinctures standardized uniformly well. So far as can be recalled all batches closely approximated in dosage 0.15 of one cat unit (0.15 cc) per pound of the patient's body weight with three exceptions, two of which were weaker, standardizing to a dosage of 0.17 cc and the other to 0.10 cc per pound of the patient's body weight. Emphasis has been placed upon the point of careful percolation in the preparation of the tincture together with the caution to use the entire contents of the sealed cans, since it has been believed to be the common practice of pharmacists to make up their tinctures of digitalis in small batches. Since a one-pound can of leaves will make ten pounds of tincture the can of leaves may not be sealed after opening and may be reopened four or five times in the course of as many weeks or months, each time with the admission of moisture and molds. Failure to observe these points has been responsible, it is believed, for many low standard tinctures as obtained in the market.

Because of closer medical observation in military organizations, patients with pneumonia were admitted to the hospital with much less delay than would have occurred under similar conditions in civil life. There were comparatively few instances of delay in admission during the initial stage of the disease, and these were due to the desire on the part of the soldiers to minimize or conceal sickness in order to keep up with the training. The dosage was administered as follows:

If the tincture in use standardized to 0.15 cc per pound of weight and the patient weighed about 160 pounds he received a total dosage of 24 cc. This was usually given in 4 cc doses every four hours for six doses. Administration was then stopped. This plan was not followed if the patient had received digitalis medication in any form during a period of ten days preceding. As a rule there was no marked slowing of pulse-rate after such doses had been given. This was in accord with the observation of Cohn[8] that slowing of the pulse-rate was not a primary effect of digitalis in therapeutic doses in hearts with normal sinus rhythm. There were but few instances of nausea, which occurred as a toxic effect when enough had been given in susceptible individuals to physiologically affect the medullary center. Partial heart-block of transitory duration occurred but once and coupled beats or frequent premature contractions as evidence of toxic effect were not common. If present these symptoms usually promptly subsided when atropin in 1–100 to 1–75 grain doses were given. A transient rise of blood-pressure

[8] Jour. Am. Med. Assn., October 30, 1915, **65**, 1527.

sometimes occurred. In one instance the systolic blood-pressure reached 190 mm. There was, as a rule, less change in the diastolic pressure. Diuresis was the most constant evidence of absorption and effect. Since fluids were forced as part of the treatment during the fever to prevent dehydration and blood concentration, the diuretic effect of digitalis in the absence of edema was, however, difficult to determine in many patients.

If further dosage were believed necessary, after four or five days, because of the clinical evidence of a dilated heart, the earlier amounts were supplemented by intravenous injection of digipuratum when obtainable, by digitalone or by the oral use of Nativelles's crystallized digitaline. O the latter preparation the dose required for full effect was 1 granule per 10 pounds of the patient's weight, providing no other form of digitalis had been given during the preceding ten days. If used to supplement the dosage of the tincture, as outlined above, not over one-half the estimated number of granules were given. Those interested in the use of standardized preparations for digitalis administration should consult the articles of Eggleston.[9]

TABLE IV.—PNEUMONIA MORTALITY.

Period.	Cases.	Deaths.	Per cent.	Remarks.
Oct. 18, 1917, to Jan. 15, 1918	...	...	....	Incidence of sepsis = 23.6 per cent.
With sepsis	66	61	92.4	Digitalis not routinely used.
Without sepsis	213	55	25.8	
	279	116	41.5	
Jan. 16, 1918, to May 18, 1918				
With sepsis	134	69	51.5	Incidence of sepsis = 22.6 per cent.
Without sepsis	458	54	11.8	Digitalis used.
	592	123	20.7	
June 1, 1918, to Dec. 31, 1918				
With sepsis	83	31	37.3	Incidence of sepsis = 24.8 per cent.
Without sepsis	251	22	8.7	Digitalis used.
	334	53	15.8	

The Results of Digitalis Therapy. Digitalis therapy in pneumonia was carried out in this manner because it was believed that circulatory failure had occurred in about one-fourth of the deaths, in which sepsis had not appeared to be a factor, for the period immediately preceding October 18, 1917, to January 15, 1918.[10]

[9] Arch. Int. Med., July, 1915, **1**, 16. Jour. Am. Med. Assn., March 13, 1920, **74**, 733.

[10] Phillips, Bruce G., Bliss, Walter P., and Stone, Willard J.: Arch. Int. Med., October, 1918, **22**, 409.

It will be noted in Table IV that during this period when digitalis was not routinely used, 55 deaths, without evidence of sepsis, occurred among 213 pneumonia patients; that is, 25.8 per cent of the deaths were believed to have been associated with cardiac failure. This belief was found upon a clinical review of many of the histories and upon the autopsy findings. Cohn[11] had previously expressed the opinion that digitalis acted the same in pneumonia as in non-febrile conditions. It should be mentioned that Type I antiserum was used intravenously in all pneumonia infections due to Type I pneumococcus, and that through the kindness of Dr. Preston Kyes, of the University of Chicago, we were supplied with his antipneumococcus chicken serum, which was used in the treatment of many patients with pneumococcus infections of other types.

With due regard for the pitfalls of statistical comparisons an attempt has been made to analyze the figures shown in the preceding table. It will be observed that during the period when digitalis was first used (January 16 to May 18) there was a decrease in the number of deaths believed to have been associated with cardiac failure to 11.8 per cent and for the second period (June 1 to December 31) to 8.7 per cent. The point may be raised that each of these intervals may have covered different phases of virulence of or susceptibility to the organisms responsible for the disease. Other unknown factors may have influenced the results, but it may be mentioned that a remarkable constancy of infective types was present from month to month during these periods. For example, it was shown[12] that among a series of 310 empyema operations (subsequent to pneumonia) during these periods streptococcus (largely hemolyticus) and pneumococcus infections were responsible for the condition as follows:

TABLE V.—INFECTIVE ORGANISMS ISOLATED IN EMPYEMA.

Period.	Number of cases.	Streptococcus, per cent.	Pneumococcus, per cent.
Oct. 20, 1917, to Jan. 21, 1918	71	73.2	26.7
Jan. 12, 1918, to Aug. 10, 1918	95	73.6	26.3
Oct. 18, 1918, to Feb. 14, 1919	85	70.4	29.4

It will also be observed in Table IV that the incidence of sepsis, as the largest single factor responsible for death also showed remarkable constancy during the one period when digitalis was not routinely used and for the two subsequent periods when the drug was used. In the first the incidence of sepsis was 23.6 per cent, in the second 22.6 per cent and in the third 24.8 per cent. It may therefore be believed that there was no marked variation in the virulence of the infection causing the disease during those compared periods.

[11] Loc. cit.

[12] Stone, Willard J.: Am. Jour. Med. Sc., July, 1919, **158**, 1.

The reduction in mortality of patients with sepsis during the last two periods (Table IV) was believed to have resulted from improvement, with increasing experience, in the method of treatment. This refers particularly to empyema. In the first period early operation was performed as soon as pus was found in the pleural cavity. This resulted in a high mortality because of collapse of the lung incident to an open pneumothorax which was many times associated with an active pneumonic process in the opposite lung. During the last two periods early aspiration was repeatedly performed followed by late operation after the activity of the pneumonic process had subsided and after, it was believed, relative immobilization of the mediastinum had occurred. Such procedure diminished the danger of an open pneumothorax when made of sufficient size to secure adequate drainage.

In connection with digitalis therapy in pneumonia it was believed rational, if used at all, to secure effect early before the heart had become incompetent through dilatation or muscle degenerative changes with consequent exhaustion of its reserve tonicity. The tincture was found by Haskell, McCants and Gardner[13] to have been better absorbed from the gastro-intestinal tract than the infusion. Cohn[14] has shown that in dogs and cats with doses of therapeutic range equal to 30 per cent of the calculated lethal dose, digitalis increased the contractile function of the cardiac muscle, and by so doing increased the volume output. In pneumonia any treatment which would beneficially affect the volume output of the heart would be highly desirable, since Hoover[15] has shown that oxygen unsaturation existed to greater or less degree in every pneumonic consolidation, a condition augmented by shallow breathing, diaphragm immobility and asynchronism, all of which would tend to interfere with an adequate blood supply to the cardiac and respiratory centers in the medulla.

Pardee[16] has shown that the body disposed of digitalis at an average rate of about 1.3 cc of the tincture per day. In many digitalized pneumonia patients of this series when it was believed four or five days later, upon clinical evidence, that more of the drug was indicated, 20 to 25 per cent of the earlier estimated dosage was additionally given with the point in mind that elimination had disposed of such an estimated proportion of the total amount. If digitalis should be used in pneumonia it would seem futile to give it routinely in doses of five minims of the tincture by mouth three or four times daily, as has been advocated by various authors. A carefully made tincture from potent leaves may be estimated, without standardization, as having an average activity of 100 mg. to the cat unit. Since

[13] Arch. Int. Med., 1916, **18**, 235.
[14] Tr. Am. Soc. Clin. Investig., Jour. Am. Med. Assn., 1920, **74**, 1597.
[15] Jour. Am. Med. Assn., September 14, 1918, **71**, 880.
[16] New York Med. Jour., December 27, 1919, No. 26, 110.

the total amount required for effect may be taken to equal 0.15 of one cat unit (0.15 cc) per pound of body weight a total dosage of 24 cc would be required for an adult of 160 pounds. If it is assumed that five minims equal 0.3 cc it will be readily seen that 80 doses would be required. Eighty doses of five minims four times daily would require twenty days for completion, a condition approximating absurdity if definite prompt digitalis effect were desired. On the other hand, after digitalization by full dosage has been secured, perpetuation of the effect, after a week or ten days, may be secured by the administration of smaller doses equaling the amount Pardee[17] has shown the body eliminates daily, that is, 1.3 cc (approximately 20 minims). It has been difficult to understand how clinicians have been able to assure themselves of definite digitalis effect from such small doses as those mentioned above, except when used to supplement full dosage given earlier. Eggleston[18] has mentioned certain safeguards in administration by this method to which I wish to subscribe. They were briefly as follows: Caution should be used in administering large doses if the patient had received digitalis in any form during the preceding ten days; nausea or vomiting, except when due to splanchnic congestion, present before treatment was begun, should stop the dosage, as should also a decrease in the heart-rate to 60 or below per minute. The drug should be stopped if frequent premature contractions, definite heart-block or coupled beats occur.

The writer has been under obligation to Dr. Ezra Bridge for painstaking assistance and verification of the autopsy records used in the compilation of the statistics.

Summary. 1. An analysis of the data secured by the study of 1205 patients with lobar and bronchopneumonia has been attempted with reference to the digitalis therapy.

2. Two hundred and seventy-nine patients with pneumonia did not receive routine digitalis therapy while 926 patients received full dosage of a potent tincture standardized by the cat method of Hatcher.

3. The gross heart-muscle changes as shown in 259 pneumonia autopsies have been described together with the microscopical study of 71 heart-muscle sections.

4. The influence of these changes upon the probable cause of death has been discussed together with the benefit believed to have been secured in treatment by the use of digitalis.

Conclusions. Sepsis in pneumonia was the most serious complication and the most frequent cause of death in the subacute or chronic forms of the disease; that is, among those who died as late as the fourteenth day of illness or subsequently. Among 283 patients in whom sepsis occurred there were 161 deaths, a mortality rate of

[17] Loc. cit. [18] Loc. cit.

56.8 per cent, while among 922 pneumonia patients without sepsis there were 131 deaths, a mortality rate of 14.2 per cent.

2. Among the causes other than sepsis responsible for death in many acute forms of the disease, cardiac-muscle failure appeared to have been a prominent factor.

3. Right ventricle dilatation was found to have occurred in 39.4 per cent of 89 lobar pneumonia autopsies and in 36.6 per cent of 112 bronchopneumonia autopsies.

4. Parenchymatous, fatty and hyaline degeneration or evidences of inflammatory reaction in the heart muscle were found in 79.3 per cent of the sections from 34 lobar pneumonia autopsies and in 59.4 per cent of the sections from 37 bronchopneumonia autopsies. The extent of these changes when considered with the right ventricle dilatation was believed in many instances to have been responsible for the circulatory failure which had occurred. In other instances the extent of the degenerative changes was less marked; in the absence of dilatation of the ventricles it appeared doubtful whether these changes, in the degree found, could have so disturbed function as to produce death.

5. The mechanical obstruction to the pulmonary circulation in extensive or massive consolidation was apparently a factor of great importance in producing right ventricle dilatation.

6. Among 213 patients without sepsis in pneumonia who were not treated by the early routine administration of a standardized tincture of digitalis the percentage of deaths believed to have been associated with cardiac failure was 25.8.

7. Among 709 patients without sepsis in pneumonia who were treated by the early routine administration of a standardized tincture of digitalis the percentage of deaths believed to have been associated with cardiac failure was 10.7.

8. The susceptibility of certain individuals to digitalis action in small dosage should be borne in mind, particularly those who manifest myocardial sclerotic changes. It should be given in large doses to elderly pneumonia patients with caution.

IMMEDIATE RECOVERY FROM EARLY DIABETES INSIPIDUS AFTER LUMBAR PUNCTURE. REPORT OF A CASE.

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Very few instances of complete recovery from diabetes insipidus after lumbar puncture have been recorded in medical literature. We are accustomed to regard the polyuria and polydipsia which so frequently accompany disturbances of the pituitary gland as

symptoms of gradual, insidious onset associated with skeletal, metabolic and sexual changes. A dysfunction of this gland structure resulting in such fundamental anatomical and physiological perversions would of necessity be of long standing, and there is no doubt that most lesions of the pituitary gland are traumatic or neoplastic in origin; are more or less destructive in nature; and are accompanied by years of functional disturbance. On the other hand, suppression or alteration of pituitary function might result from the presence of an acute inflammatory process with plastic exudate or from a transient edema of the pituitary gland. Such a transient condition might account for the gradual or rapid cure of diabetes insipidus which occasionally follows the lowering of intracranial pressure by spinal puncture. Such pathological conditions of the pituitary gland may include all grades of glandular disturbance from an acute hemorrhagic infection with rapid death to a simple and transient edema. The former condition can be diagnosed correctly only at autopsy and the latter by its transient character and the early results of therapy.

The majority of investigators agree that a secretion from the pars intermedius and pars posterior of the pituitary gland in some manner or other exerts a restricting influence upon the volume output of urine. Should we accept the theory of Dr. Harvey Cushing and his associates that the pituitary secretion reaches the third cerebral ventricle by way of the infundibulum cerebri, then we can conceive that an obstruction to the flow would be produced by a local edema or by a plastic exudate and that a like obstruction would result from increased intracranial pressure due to any cause. In other words, an increased turgescence of the infundibular stalk or the back pressure from either a mild or severe hydrocephalus could act as a partial or complete obturator to the secretory flow from the pituitary gland. Even if one accepts this hypothesis, however, why a transient disturbance of pituitary function with diabetes insipidus does not commonly occur or is not more frequently recognized, remains a mystery.

Before reporting the author's case it is of interest to offer a *resume* of three cases reported in the literature, in each of which striking results followed a lowering of the intraspinal and hence of the intracranial pressure.

1. In a case reported on June 22, 1916, by Dr. Evarts Graham,[1] diabetes insipidus had existed for about two months before the patient was examined. The patient, a male, aged twenty-four years, could assign no cause for the disturbance except a blow on the chest suffered about a month and a half before the onset of polyuria. On lumbar puncture the fluid was found to be under markedly increased pressure—shooting out in a steady stream for

[1] Jour. Am. Med. Assn., 1917, **69**, 1499.

a distance of from eight to twelve inches. Following this procedure the patient was bedridden for four days with a severe headache. At the expiration of this period he went home but returned to the hospital for five days, during which period the headache gradually disappeared. The polyuria ceased shortly after the intracranial pressure was relieved. The patient's progress after leaving the hospital was not noted.

2. A case of diabetes insipidus of four years' duration was reported by Dr. J. B. Herrick[2] in July, 1912. The patient, a male, aged forty-three years, complained of marked thirst and frequent urination. During spinal puncture the fluid escaped very slowly under low pressure, and less than 5 cc were withdrawn. This procedure was followed by great prostration, with severe headache and pain in the back of the neck, associated with anorexia, vomiting and general malaise. The pain was so intense that morphine was given. When the prostration disappeared and fluid and food were again freely taken the thirst and the output of of urine were found to be normal. Likewise, frequent attacks of petit mal which existed prior to lumbar puncture disappeared; however, Dr. Herrick was informed by the family physician three months later that these symptoms were returning.

3. A case of diabetes insipidus of about one year's duration, which had been relieved by spinal puncture, was reported recently by Dr. P. J. Cammidge.[3] The patient, a male, aged forty-two years, had been troubled with marked thirst and polyuria for fully a year before examination. About one ounce of spinal fluid, under great pressure, was removed with a needle. This event was followed by a severe headache which persisted for four days. The frequent urination rapidly disappeared, so that in a week or two the nocturnal urination had ceased. There was no recurrence of symptoms after six years.

The author's case, a male, aged twenty-seven years, was referred by Dr. R. G. Pearce, of the department of health of the B. F. Goodrich Company, Akron, Ohio. The patient came in for examination on November 26, 1920, complaining of the frequent voiding of large quantities of urine associated with great thirst. Abdominal discomfort resulting from a full bladder, had awakened him at 4 o'clock on that morning. This was immediately relieved after urination, but he was obliged to empty his bladder twice more before 6 A.M., and each time he passed a large amount of urine. Thereafter he voided copiously about every twenty minutes, even retiring frequently for relief during the physical examination.

Another symptom which persisted from the time of onset was a heavy "dry" feeling behind the bridge of the nose. As he stated it, "I feel as if trouble here is causing my thirst." He also noted

[2] Arch. Int. Med., 1912, **10**, 1–7.
[3] Practitioner, 1920, **105**, 244–247.

marked sweating of the body, hands and feet, so that a wet undershirt and soaked stockings and shoes made him feel as if he had fallen into a pool of water. Aside from these complaints the patient felt as well and active as ever, with no headache, disturbance of vision or real pain anywhere.

Past History. The patient had had typhoid fever at the age of ten years. In January, 1918, he was under observation for pulmonary tuberculosis, but was eventually discharged as negative. However, for the sake of safety, he went West for a couple of years and lived outdoors. He acquired influenza in February, 1920, but made a good recovery. Since then his health had been excellent. There was no history of venereal infection. He had been married four years. His wife and one child were living and well.

Family History. The patient's father and mother were living and well. He had four brothers and sisters, all living and in normal health. There had been no history of tuberculosis, insanity or diabetes in the family. All his grandparents lived to be over seventy-five years of age, except the paternal grandmother, who died at the age of fifty-seven years, cause of death unknown.

Physical Examination. The author's examination of the patient made four hours after the onset of the polyuria may be summarized as follows: Temperature, 97°; pulse, 70; respirations, 20; patient of medium size and build, well-developed and well-nourished, with no apparent loss in weight; mental condition alert with no undue nervousness; marked sweating of hands, body, legs, and feet, but none on the face or the neck; the shirt, stockings and shoes were soaking wet.

Head. No tenderness over the sinuses; slight ptosis of the left upper eyelid; visual fields normal to the finger test, but perimetry revealed slight concentric narrowing in the left eye; no external ophthalmoplegia; pupils equal, regular, centrally placed and reacting well to light and accommodation; vision normal by Snellen's test card; septum of nose markedly deviated to the left with absence of sense of smell on that side; slight hyperesthesia to cotton wool over the distribution of the left fifth cranial nerve; facial muscles and those of mastication negative; hearing in the left ear definitely diminished to a watch tick, with a lessened bone conduction; eardrums normal; tongue protruding in the midline; speech normal; power in sternocleidomastoids and trapezii muscles equal on both sides; teeth and tonsils negative; no evidence of increased salivation or lacrimation.

Thyroid gland palpable but not enlarged. All lymph glands of normal size.

Thorax symmetrical, expansion of upper and lower ribs as well as flaring of subcostal margins symmetrical.

Lungs negative.

Heart of normal size; no adventitious sounds; rate, 70.

Pulse rhythmic, regular, symmetrical, synchronous, with normal anacrotus and katacrotus.

Blood-pressure. Systolic, 134; diastolic, 84. Abdomen and genitalia negative.

Reflexes. Biceps, triceps, patellar and tendo Achillis equal and active; corneal, epigastric, abdominal, cremasteric and plantar reflexes all symmetrical and normal; no sensory disturbance in the skin except as noted above in the distribution of the left fifth cranial nerve; no Romberg, Babinski, Chaddock or Oppenheim; no acro- or approximo-ataxia in the upper or the lower extremities; no dysdiadokokinesia.

Urine. 2000 cc passed between 11 A.M., and 1 P.M., on the first day; clear; faint; yellowish tinge; acid; specific gravity, 1000; albumin, none; sugar, none; microscopical examination, negative.

Roentgen-ray Examination. Sella turcica normal in size and contour; skull negative for visible tumor; facial sinuses all of normal density; teeth, no caries or apical abscesses.

Eye-grounds. Left nerve-head more pale than normal, otherwise normal.

Blood Count. Red corpuscles, 5,800,000; white corpuscles, 7200; hemoglobin, 100 per cent (Tallquist).

On the second day the patient was referred to Lakeside Hospital and placed under the care of Dr. C. D. Christie. From 4 P.M., of that day to 7 A.M., of the following day the urinary output was 4100 cc, with a fluid intake of 5970 cc.

A lumbar puncture for diagnostic purposes was performed two days later, on November 30, 1920, four days after the onset of the symptoms. Eight cc of clear spinal fluid were removed under *normal pressure.* Examination of the spinal fluid showed a cell count of 2 mononuclears per cubic millimeter; globulin, negative (Noguchi, Pandy and Ross-Jones); Wassermann test on blood and spinal fluid, negative. Phenolsulphonephthalein output of kidney (after spinal puncture) amounted for the first hour to 100 cc (40 per cent), for the second hour to 500 cc (17 per cent), making the total for two hours 600 cc (57 per cent).

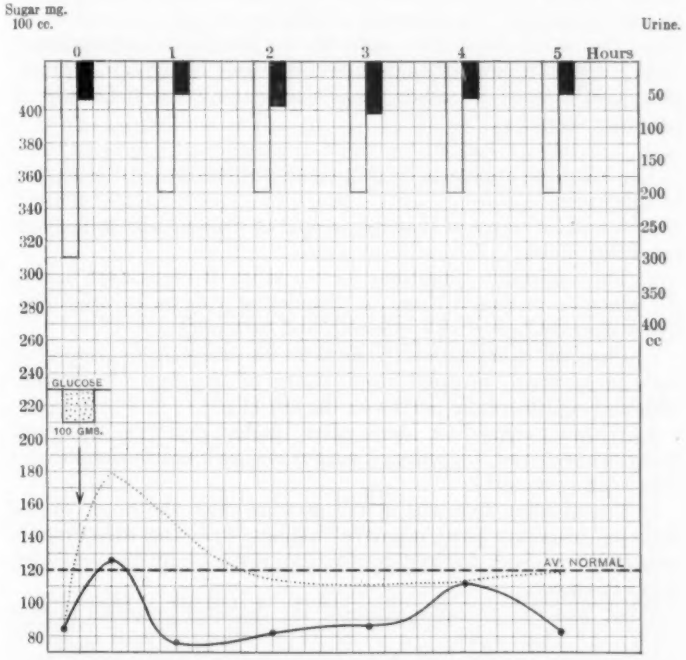
Two days later the Mosenthal nephritic test was made, showing the specific gravity of the day urine to be 1020 to 1026; of the night urine, 1032; with a total urinary output during the day of 306 cc, and during the night of 100 cc, and a liquid intake for the twenty-four hours of 1200 cc.

Thus on the second day after lumbar puncture the total urinary output for twenty-four hours was 406 cc as compared with 4100 cc during fifteen hours before the lumbar puncture; while the fluid intake during the latter period was 1200 cc as compared with 5970 cc during the first cited period. The specific gravity of the urine showed a corresponding alteration from 1005 and

1006 before the spinal puncture to 1030 immediately after, remaining at from 1026 to 1030.

The temperature was increased to 100° and 101° F. on the second and third days after the lumbar puncture, returning to normal on the fourth day.

For five days after the removal of the subarachnoid fluid the patient had a severe headache, and he was troubled with insomnia and did not feel physically fit for a period of twenty days. Dur-



Blood-sugar curve typical of hypopituitarism shown by author's case. (Compare with normal curve shown by dotted line.) The black oblong spaces at the top indicate urinary output; the uncolored oblongs indicate water intake.

ing this time the neurological signs gradually subsided and neither then nor since was there any recurrence of the polydipsia or polyuria. About two weeks later he developed herpes on both the upper and lower lips following an acute rhinitis. This was followed in a few days by pain under the right eye. Roentgenographs of the sinuses showed a dense clouding of the left antrum. This was tapped and a large amount of pus evacuated. Within a week

after irrigation of this sinus was begun the patient felt as well as ever and all of his neuralgic pain disappeared.

A careful examination of the patient on May 3, 1921, five and a half months after the onset of diabetes insipidus, gave normal findings throughout. He has been well and very active for over four months and has had no recurrence of his thirst or frequent urination since the spinal puncture made four days after the onset of the polyuria. The chart shows the curve of sugar tolerance at the date of this last examination. There was no hyperglycemia at any time after the ingestion of 100 gm of glucose, and at its peak the blood sugar rose only to the maximum normal level. This curve is typical of that shown by cases of hypopituitarism. However, there is no other present indication of a deficiency of pituitary secretion.

The following appear to be the significant features in the history of this patient:

1. A sudden onset of diabetes insipidus without any immediate preceding illness.
2. The subjective symptoms were a sense of discomfort behind the glabella, increased thirst, a disquieting volume in urine output and marked sweating of the body and extremities.
3. Physical examination confirmed the subjective symptoms, and, in addition, revealed involvement of the first (?), second, fifth and eighth cranial nerves on the left side.
4. Within twenty-four hours after lumbar puncture the great thirst was relieved, the urinary output was reduced to normal and the sweating ceased.
5. Examination five and a half months after the onset of the diabetes insipidus gave negative findings with the exception of laboratory evidence for hypopituitarism, revealed by the very high sugar tolerance.

What was the probable cause of the diabetes insipidus in this case? (*a*) That it was not an acute infectious process is shown by the absence of fever, leukocytosis or any other symptom prior to the spinal puncture; (*b*) that it was not a brain or pituitary tumor is shown by the absence of increased pressure of the spinal fluid and the absence of choked disk in either eye, together with the magical subsidence of symptoms after the puncture and the non-recurrence in five and a half months; (*c*) the hyperidrosis undoubtedly resulted from a transient stimulation of the bulbar-autonomic or higher centers of sweat control.

In view of these facts it seems probable that in this case the disturbance was due to a serous meningitis with edema of the infundibulum cerebri and involvement of certain cranial nerves on the left side. The removal of 8 cc of subarachnoid fluid, even though this was under normal pressure, was adequate to restore

proper circulatory equilibrium. While this conclusion is of necessity entirely speculative, nevertheless the fact remains that whatever the pathological process may have been, it was sufficiently mild in character for complete relief to be secured.

Conclusions. 1. Diabetes insipidus may result not only from destructive lesions of the pituitary gland but from any cause which may obstruct the flow of the normal secretion.

2. Such an obstruction may result from a transient edema of the pituitary gland or from an inflammation with resultant plastic exudate, or it may result from extrapituitary conditions, such as increased intracranial pressure from any cause.

3. The withdrawal of spinal fluid, whether under high or low tension, tends to relieve this pressure and to remove the obstruction.

4. The experience of the author, in whose case there has been no recurrence of symptoms five and a half months after no other treatment than lumbar puncture, indicates that in any case of diabetes insipidus the patient should be given the advantage of the possibility of early relief by this means.

THE CLINICAL, BACTERIOLOGIC AND PATHOLOGIC FINDINGS IN A CASE OF INFLUENZAL MENINGITIS.

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and

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Apparently the first authentic case of influenzal meningitis was reported by Slawyk,[1] in 1899, working under the direct supervision of Pfeiffer. Occasional cases occurring thereafter are described in the literature. Writing in 1910, Simon[2] collected 12 instances of this disease.

Martha Wollstein,[3] in 1911, produced in monkeys lesions simulating influenzal meningitis. She made a review of the literature, tabulating 49 cases of pure influenzal infections. Torrey,[4] Dunn[5 6] and Koplik[7] added 30, 4 and 6 cases respectively. Stone[8] summarized 13 others and reported a case of his own in 1920. Early in 1921, Neal[9] again reviewed the literature and discussed 32 cases, previously unreported. Since the time of her paper there have been recorded but 2 authentic instances of uncomplicated influenzal infection of the meninges, these being described by Litchfield[10] and Caprario.[11]

There have been, as far as we have been able to determine, 150

cases reported. We wish to submit, in addition, the following record:

This case came under observation on the medical service of the Infants' Hospital on June 12, 1921.

Family History. Essentially negative throughout. The patient was the last of six normal pregnancies. There was no history of exposure to tuberculosis or recent contagious disease or "colds" in the family.

Past History. Full term at birth and delivery was normal.

Feeding. Entirely breast-fed for six months, after which the infant was started on the ordinary infants' diet in addition to breast-feedings, which have been continued until the present. Has gained normally in weight throughout, without evidence of digestive difficulty until the beginning of the present illness.

Development. Sat up alone at five months; walked at ten months and said a few short words at fifteen months. Dentition normal.

Illnesses. No previous illness.

Present Illness. Nine days before admission the baby had a "bad cold," with a nasal discharge, sneezing and slight cough, which continued with diminishing severity for five days. He had apparently completely recovered, when two nights ago he awoke with a "high fever" and vomited small amounts of breast milk on two occasions. Was restless and cried a great deal, and had a pronounced thirst. There has been no further vomiting, but the child has taken feedings very poorly and the bowels have been markedly constipated. He turned constantly from side to side and grunted with pain when handled. There has been no noticeable retraction of the head. He was seen by the local physician, who diagnosed the case as "epidemic meningitis," and was referred to the hospital.

Physical Examination. Well-developed and nourished male infant of seventeen months, without noticeable loss of subcutaneous fat. He dozed frequently during the examination but awakened with a cry of pain when any attempt was made to flex the neck or manipulate the lower extremities. There was cervical adenitis, but no deformity of the bones or the joints.

Head. Showed both fontanelles completely closed with no external evidence of hydrocephalus.

Facies. Apathetic; cheeks flushed.

Eyes. Pupils reacted normally to light, equal and regular. There was no conjunctival discharge.

Ears. Showed no discharge, but on otoscopic examination a pair of markedly injected drums were disclosed, with pronounced bulging in the posterior-superior quadrant.

Nose. Showed purulent discharge.

Mouth. Teeth were normal; mucous membranes flecked with sordes. There was no injection, exanthemata or exudate.

Throat. Tonsils were moderately hypertrophic and moderately injected.

Neck. There was pronounced tenderness on attempted flexion with moderate rigidity; there was no retraction and with prolonged manipulation the chin could be pushed forward on to the chest wall.

Chest. Was symmetrical. Expansion was equal on both sides. No rosary.

Lungs. Were essentially normal throughout to auscultation and percussion; no increase in spinal or interscapular dulness.

Heart. Action was rapid and regular; sounds were of good quality; no murmurs or thrill made out, and there was no enlargement to percussion.

Abdomen. Liver was barely palpable. Spleen not made out. There were no masses, rigidity or tenderness.

Extremities. Were negative throughout.

Reflexes. Patellar jerks were not obtained. Achilles reflexes were sluggish; no Babinski, ankle-clonus or Kernig. There was a typical Brudzinski sign with some tendency toward flexion of the thigh on the trunk, with the neck as described, otherwise the deep and superficial reflexes were normal.

Skin. Normal.

Diagnosis of acute otitis media (bilateral) and meningitis (type undetermined) was made at that time.

Lumbar puncture was done immediately, at which time 8 cc of a distinctly turbid fluid was obtained under moderately diminished pressure. There were 2500 cells per cu. mm., 85 per cent of which were of the polymorphonuclear variety and 15 per cent lymphocytes. Globulin test was strongly positive.

Double paracentesis was performed and pus was obtained in large quantities from both ears, smears of which revealed no organisms and cultures from which gave no growth in seventy-two hours. 10 cc of antimeningococcus serum were administered at this time.

During the succeeding twenty-four hours there was no definite change in the symptoms, except that he seemed to be slightly brighter.

June 13. Second lumbar puncture was done and 25 cc of a similar fluid were obtained under slightly increased pressure. Cell count had fallen to 1100 per c.mm., of which 65 per cent were polynuclear leukocytes. Globulin test continued positive. There was no reduction of Benedict's solution. 15 cc of antimeningococcus serum were administered at this time.

June 13. The urine was yellow and cloudy. It contained albumin, large trace; sugar, 0; few red and white blood cells; no casts.

June 15. Third lumbar puncture was done and 40 cc of a similar fluid were obtained under definitely increased pressure. Cell count, 1910. Globulin positive. Benedict's solution was not reduced. 30 cc of meningococcus serum were administered at this time.

June 15. Blood: White blood count, 22,800.

June 17. Fourth lumbar puncture was done and 25 cc of similar fluid was obtained, which clotted almost instantaneously, making a cell count unsatisfactory; but there was definitely more purulent fluid than on the previous taps and the cells and organisms were increased in number.

Following the fourth lumbar puncture, which showed a decidedly purulent fluid, with a pronounced progression in turbidity, since the previous day, further lumbar puncture was thought to be futile and the treatment from that time on was symptomatic. The temperature maintained a level between 103° to 104° F. and the usual signs of meningeal irritation (Kernig, Brudzinski and neck rigidity and retraction), which were not pronounced on entry, became more marked. He grew very irrational, requiring sedatives for control. There was a marked dyspnea and the patient died on the morning of June 21, his ninth day in the hospital.

Bacteriologic Report. Smears of the spinal fluid made at the time of admission, and repeated four times before death, showed large numbers of both intra- and extracellular organisms having the characteristics of Bacillus influenza. At autopsy similar organisms were found in direct smears from the brain, cord and middle-ears. Culture of the heart's blood likewise showed them. There were no demonstrable differences between the bacilli obtained from the different organs. All grew well on blood agar but could not be grown on media without blood.

Morphology. The bacillus was Gram-negative and non-motile. In direct smears from spinal fluid and exudate it showed marked pleomorphism. There were many small thin bipolar staining bacilli of the so-called typical influenza type, but in addition to these there were long forms and filaments, and a thick variety (probably an involution form) which was both long and short, straight and curved. In many fields the differences in size, shape and arrangement reminded one of preparations of Bacillus coli. This pleomorphism persisted throughout five weeks' cultivation on artificial media and was increased by passage through a guinea-pig.

In addition to the differences present in the early smears, culture on blood agar brought out striking involution forms. Only the youngest cultures showed the morphology usually thought of as characteristic of the influenza bacillus. In from twelve to twenty-four hours there developed bizarre forms which were very thick, long and curled.

Cultural Features. Repeated unsuccessful attempts were made to grow the organism on plain agar, blood serum and starch agar. It could be grown only on blood agar or plain agar smeared with blood. Human blood agar proved to be a much poorer medium than that made with a guinea-pig's or a rabbit's blood. Intentional contamination of the blood plates with staphylococcus, Bacillus

coli and Bacillus subtilis did little to facilitate growth and in some cases actually inhibited it. An unsuccessful attempt was made to grow the bacillus on plain agar in symbiosis with Bacillus coli.

The colonies were at first of the dew-drop, pin-point variety, but after two or three days took on a slightly milky appearance. Individual colonies seldom grew to be more than 1 mm. in diameter, and were round, smooth and amorphous, with very finely irregular edges. By inoculation into starch blood agar, colonies were obtained which were 5 mm. in diameter and had slightly elevated but not lobulated edges.

Biochemical Features. The bacillus was non-hemolytic. It produced indol in both peptone and plain blood broth and reduced nitrates to nitrites. In brom-cresol-purple blood-broth milk there

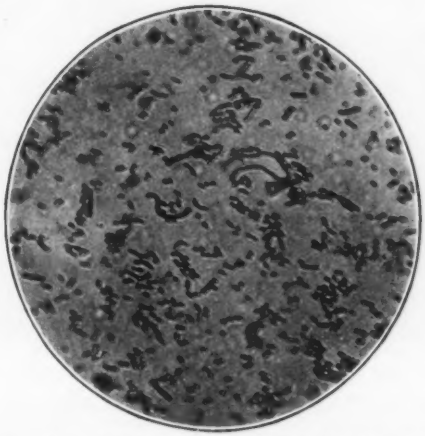

FIG. 1.—Photomicrograph (oil immersion). Twenty-four-hour culture showing involution forms grown on rabbit blood agar.

was slight but definite acidity in twenty-four to forty-eight hours, with questionable alkalinity later. It did not form amylase in starch agar media.

Pathogenicity. After the organism had been cultivated artificially for four weeks 4 cc of a twenty-four-hour blood-broth culture were injected intraperitoneally into a guinea-pig. The animal died in twenty-six hours and on autopsy showed an acute fibrinous peritonitis. Pure cultures of Bacillus influenzæ were recovered from the peritoneal exudate and the heart's blood.

Post-mortem Examination. Autopsy was performed six and a half hours after death.

Anatomical diagnosis: Acute purulent leptomeningitis (Bacillus influenzæ); internal pyocephalus with acute ependymitis; septi-

cemia (Bacillus influenzæ); suppurative otitis media, bilateral; thromboses of the superior longitudinal and both lateral sinuses; acute bronchitis; edema and congestion of the lungs and infarctions of the lungs. The body was well developed and nourished, with unequal pupils. There was nothing remarkable in the body.

The important changes seen were in the brain. It weighed 1140 gm. and showed in addition to thrombi in the sinuses a thick greenish exudate beneath the pia mater. This was generally distributed over the lateral surfaces, most extensive near the Rolandic fissures. Here, besides filling the sulci, it extended over several convolutions, presenting patches 2 to 3 cm. in diameter. In other portions there were linear extensions of the exudate. In making cover-glass preparations the exudate was fully 1 mm. thick. It was quite firm, elastic, having practically the consistency and elasticity of a fibrinous exudate. The brain was quite plastic and the convolutions markedly flattened, the sulci being obliterated, and there was intense congestion, especially of the larger veins.

A view of the base of the brain presented a similar exudate, slightly softer, darker green and 3 to 4 mm. in thickness. It covered the medulla, pons, inferior surface of the cerebellum and an area surrounding the optic tracts, with a diameter of about 4 cm. Whereas the surface of the brain was dry on lifting it from the base of the skull and upon incising the tentorium cerebelli a large amount of thin, whitish, puriform fluid escaped from the spinal canal.

A horizontal section of the brain, exposing the lateral ventricles, showed them to be greatly dilated and containing a thick deposit of fibrinous material, especially in the posterior horns. There was destruction of the ependyma and excavation into the white matter, particularly the posterior portions. The brain as a whole was deeply injected and in the basal ganglia, especially the lenticular nucleus, the color was pink and there were apparently punctate hemorrhages. The structures bounding the third ventricle were collapsed and had probably been destroyed by the inflammatory process.

Both middle-ears contained a puriform exudate. The dura mater of the spinal cord was distended. Upon reflection the cord was covered with a thick, firm, greenish exudate similar to that seen on the cerebrum. It was about 2 mm. thick and appeared to completely envelop the cord.

Microscopic Examination. Many sections of the cortex and meninges show a purulent exudate beneath and distending the pia arachnoid. It consists of numerous polymorphonuclear leukocytes, many being disintegrated, a small amount of fibrin and a moderate number of large mononuclear phagocytes (endothelial leukocytes). Some of the polymorphonuclears are seen in the vessel walls. The vessels everywhere in the gray matter are distended with red cells.

In other sections there is general infiltration of the perivascular spaces of the pial vessels and those of the brain substance by numerous large, endothelial leukocytes and a moderate number of lymphoid and plasma cells.

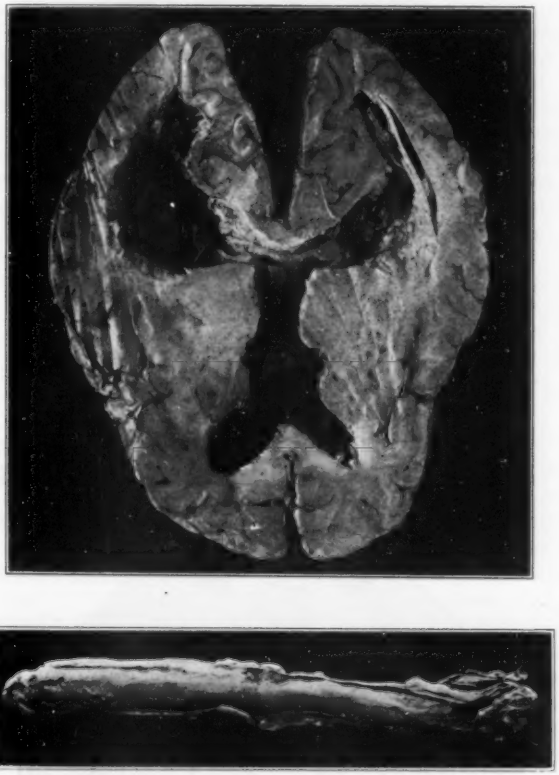

FIG. 2.—Photomicrograph of brain showing dilatation and destruction of the lateral ventricles. Below the cord is covered with a heavy exudate.

A section from the region of the lateral ventricle shows destruction, especially of the ependyma. Migrating cells are numerous, including large mononuclear phagocytes (endothelial leukocytes) many lymphoid and plasma cells, and in a few areas where the cells are vacuolated a small number of polymorphonuclear leukocytes are found. Here also there is marked perivascular infiltration.

A section of the basal ganglia shows general congestion of the vessels, many being almost entirely filled with polymorphonuclears.

There is perivascular infiltration, and along one border the brain substance has a vacuolated appearance.

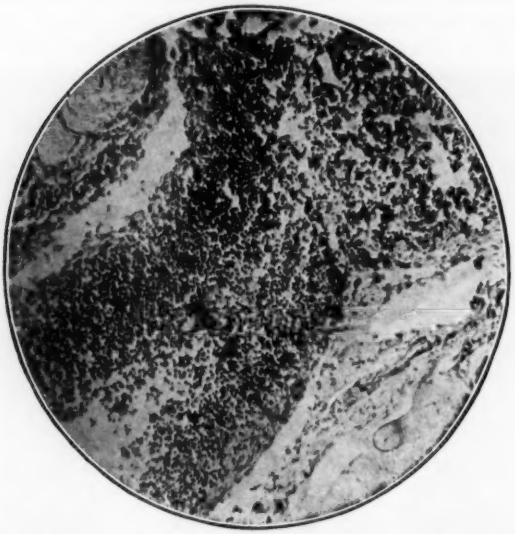

FIG. 3.—Photomicrograph (low power) showing purulent exudate enveloping spinal cord and nerve root.

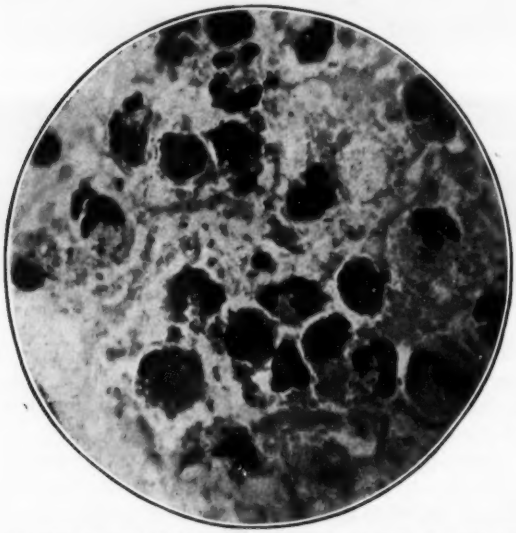

FIG. 4.—Photomicrograph (oil immersion). Smear of exudate from spinal cord showing intracellular bacilli in polymorphonuclear leukocytes.

Sections of the spinal cord show the pia mater to be distended or broken in places by a thick, purulent exudate, consisting of myriad polymorphs, many of these disintegrated and often enmeshed in heavy webs of fibrin. This exudate is extensive, involving the ventral and posterior roots as well as covering the entire cord. A Giemsa stain reveals numerous short bacilli, morphologically Bacillus influenza, both intra- and extracellular in the exudate.

A section of the Gasserian ganglion shows thrombi in many of the adjacent venous sinuses. The pituitary is normal.

Four sections of the lungs show extensive congestion and edema. Many of the vessels are filled with polymorphs. In two sections some of the capillaries have apparently ruptured, as shown by small patches of alveoli filled with red cells. There is a small infarct which includes about twelve to fifteen alveoli and a large vessel which is thrombosed. Many of the other alveoli are filled with a pale, eosin-staining, granular material. The lymphatics are dilated. The pleura is intact. In the bronchi there is infiltration of the mucosa by numerous polymorphs and occasional colonies of bacteria resembling chains of streptococci.

Sections of the heart, gastro-intestinal tract, pancreas, liver, kidneys and adrenals show little aside from congestion. The tonsils show slight acute inflammation.

Summary. The clinical picture was that of an acute meningeal infection with a positive Kernig, Brudzinski, neck rigidity, retraction of the head, fever and leukocytosis. The exact diagnosis was of necessity made through the bacteriological findings in the laboratory.

The bacillus obtained was Gram-negative, hemoglobinophilic, pleomorphic, aërobic, non-hemolytic and non-motile. Its colonies were round with finely irregular edges. Under proper conditions it produced indol, formed acid in milk, reduced nitrates to nitrites, but did not produce amylase. During five weeks of study it did not show the phenomenon of symbiosis. In a guinea-pig intraperitoneal injection was followed by peritonitis, septicemia and death in twenty-six hours.

In its morphologic and cultural characteristics the organism so described corresponds with forms isolated from meningitis cases by Slawyk, Wollstein and others. All these investigators have emphasized the pleomorphism, but in spite of it they have, with only occasional exceptions, agreed that the organism should be classed as Bacillus influenza. But it has long been felt that this name was being given to a group of Gram-negative hemoglobinophilic bacilli, which might later be differentiated into strains in some such way as the streptococci have been differentiated. It was with this end in view that the various biochemical tests were suggested by Jordan[14] and Rivers.[15] [16] As yet however, no constant differences have been found between the respiratory tract and meningeal organisms, and although the bacillus from the case reported in the present paper

gave characteristics similar to those shown by the meningeal strains with which Rivers worked, they do not differ in this respect from some of the epidemic strains or strains from normal throats. Up to the present time the more marked pleomorphism is the only difference noted in the meningeal form as distinguished from the epidemic strains, and we are as yet without an explanation of the fact that in the recent epidemics there were so very few cases of influenzal meningitis reported. It is still difficult to explain why, with the much more common occurrence of influenzal meningitis in infants and children a study of the complications of 816 cases of influenza in children made by Levin[17] at the Cook County Hospital in Chicago during the epidemic only 5 cases of meningitis should have been found, and none of these from Bacillus influenza.

Concerning treatment opinions differ. Torrey[4] summarizes the therapeutic possibilities as follows:

"I. The anti-influenzal serum of Wollstein, whose action appears to be specific. Where practicable this serum should certainly be tried.

"II. Hexamethylenamin, which has been recommended by a number of writers, notable Brem and Zeiler,[13] and by Batten. The latter reports a case in which recovery followed its use. There seems, however, to be less basis for regarding it of great value than is the case with either Wollstein's serum or repeated spinal puncture and drainage.

"III. Repeated lumbar puncture."

The last was first suggested by Quincke.

Added to the common pathologic picture of a purulent leptomeningitis described by Davis[12] there was septicemia (Bacillus influenza) and an internal pyocephalus with acute ependymitis.

We are indebted to Dr. W. W. Howell, from whose clinic the case was taken, and to Dr. V. C. Jacobson for the photographs.

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EXPERIMENTAL POLYURIA.*

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CHICAGO, ILL.

(Work done in Department of Anatomy, University of Chicago.)

This work was begun for the purpose of determining experimentally the effect of intravenous injections of extract of the pituitary gland upon the so-called polyuria of hypophyseal origin. Before it had proceeded far our attention was attracted to certain striking variations from the generally accepted ideas concerning the production of polyuria of this type, and it seemed worth while to investigate the means of producing it.

Dogs were used throughout all the experiments. Ether was used as the anesthetic, and during the operation was administered by the intratracheal method. The gland was exposed by the buccal (transpharyngeal) route, first described accurately and used successfully by Aschner. In each case the normal urine excretion for twenty-four hours was measured as a preoperative control. Synopsis of work:

* This work was made possible through the kindness and generosity of Mrs. Nettie McCormick. I also wish to express my indebtedness to Dr. R. R. Bensley, of the University of Chicago, and to Dr. Dean Lewis for their interest and encouragement, and to Mr. Siegfred Maurer for his very hearty coöperation and many valuable suggestions.

1. Stimulation of the anterior and posterior lobes of the hypophysis:
   (*a*) Varying degrees of heat.
      (1) Heated rod.
      (2) Paraffine.
   (*b*) Trauma—pinching and pulling with tissue forceps.
   (*c*) Cone-shaped plug of beeswax pushed into opening in bone.
   (*d*) Induced current—electric.
2. Herniation of gland through dural opening.
3. Traction on base of brain with as little trauma to the gland as possible.
4. Effect of pituitrin and epinephrin on polyuria.

Stimulation of the Anterior and Posterior Lobes of the Hypophysis with Heated Rod.—In this group nine animals were used. After exposing the hypophysis the gland was stimulated by traumatizing it with a metal rod heated to varying temperatures. The local effect, observed post mortem, varied from a moderate hyperemia of the anterior and posterior lobes to complete destruction of the gland. In only one instance was there observed a polyuria of any considerable extent.

For eight animals of this group the average twenty-four-hour urine measured 232 cc and 221 cc for the two days immediately preceding the operation, and 200 cc, 243 cc, 253 cc, 299 cc, 277 cc, 180 cc, 260 cc and 200 cc for the successive days after the operation. This curve of urinary excretion may be seen represented graphically in Fig. 1.

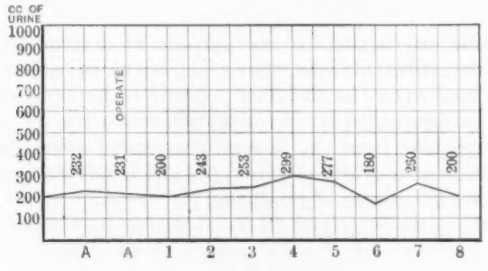

FIG. 1

In one animal of this group, dog 2, there was a marked polyuria. The daily preoperative urinary excretion was 200 cc. The stimulation consisted in trauma with a rod heated to a "black-hot" point—that is the point at which the rod appears black after cherry red has faded. The rod was 3 mm. in diameter, and was simply brought in contact with the structures at the bottom of the opening after the dura had been incised. At this stage in our work

our landmarks were not as thoroughly impressed upon us as they later were, and we were not able definitely to locate the hypophysis. During the first twenty-four hours practically no urine was voided. In the second twenty-four hours the quantity was 650 cc, and during the third twenty-four hours the amount increased to 1500 cc. At this time the dog appeared to be very sick—scarcely able to stand. It was killed at the end of the third twenty-four hours. At the postmortem examination it was found that our opening through the sphenoid bone was so far posterior that the hypophysis had not been exposed and that our stimulation had been applied to the base of the brain posterior to the hypophysis, in the region of the corpora mammillaria. The results are more conspicuously evident when shown by means of curves in Fig. 2.

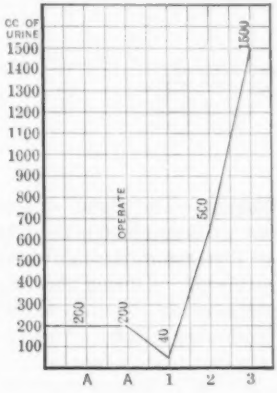

FIG. 2

Stimulation with Heated Paraffine.—In dogs 14, 37 and 39 paraffine heated to 70°, 110° and 130° C. was poured into the cavity in the sphenoid bone without otherwise disturbing the gland. In dog 37 the dura was not incised. In no instance was there any change in the amount of urine excreted.

Mechanical Trauma.—*Pinching and Pulling with Tissue Forceps.*—In dogs 10, 11 and 21 the gland was traumatized by pinching and pulling on the anterior and posterior lobes with tissue forceps. On the two days preceding the operation the average urinary output was 150 cc in twenty-four hours. During the twenty-four-hour period immediately after operation the average rose to 297 cc, after which it gradually fell until it reached 180 cc at the end of the fourth twenty-four-hour period after operation. This result may be seen graphically represented in Fig. 3.

Cone-shaped Plug of Beeswax Pushed into Opening in Sphenoid.—In dog 71*a* a cone-shaped plug of beeswax, approximately 1 cm. in

diameter at the base and 1 cm. long, was forced into the opening in the sphenoid against the hypophysis. The gland was tipped slightly forward so that the plug impinged on both the anterior and posterior lobes. The preoperative excretion had been averaging 250 cc to 300 cc daily. The postoperative excretion was slightly less, being from 150 cc to 250 cc daily. After ten days of observation the dog was apparently in normal physical condition and was used for other experimental work.

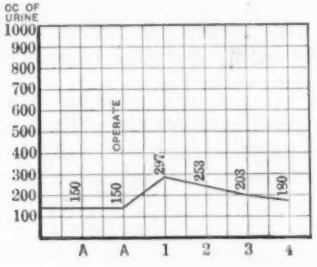

FIG. 3

Induced Electric Current.—The gland was stimulated by means of an induced current in dogs 58, 63, 66, 69*a* and 70*a*. In each instance there was an increase in the daily amount of urine. This was most marked in dog 63. During the two days preceding the operation in this experiment the urine excreted in twenty-four hours measured 300 cc. Following electric stimulation the amount increased to 1400 cc in the first twenty-four hours, 3800 cc in the second twenty-four hours and 4200 cc during the third twenty-four hours. This polyuria lasted for six days, but as the urinary output was modified by other experimental work for which the animal was used, the remaining period will be discussed later. Fig. 4 indicates graphically the extent of this change.

Herniation of the Gland through the Dural Opening.—In dog 15 the sphenoid bone was much wider than is usual and the venous sinuses surrounding the hypophysis were correspondingly formed in a larger circle. This made wider incision of the dura possible. When this step of the operation was performed the gland herniated through the dural opening, forced by a gush of cerebrospinal fluid. The degree of protrusion of the gland and the amount of cerebrospinal fluid were greatly in excess of anything previously noted. No manipulation was necessary to bring the gland well into view. A small portion of the anterior lobe was excised and the operation stopped. The dog was in excellent condition at the close of the operation. The urinary output during the three days previous to operation was 160 cc per twenty-four hours. This increased to 2360 cc during the first twenty-four hours and to 3680 cc during the

second twenty-four hours following operation. It then fell to 2140 cc in the third twenty-four hours. The dog was in excellent condition, but was killed at this time in order that the tissues might be studied during active polyuria. The excretory curve on dog 15 is shown in Fig. 5.

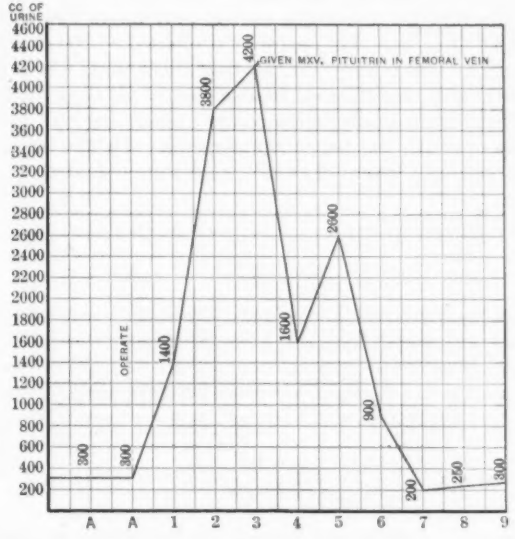

FIG. 4

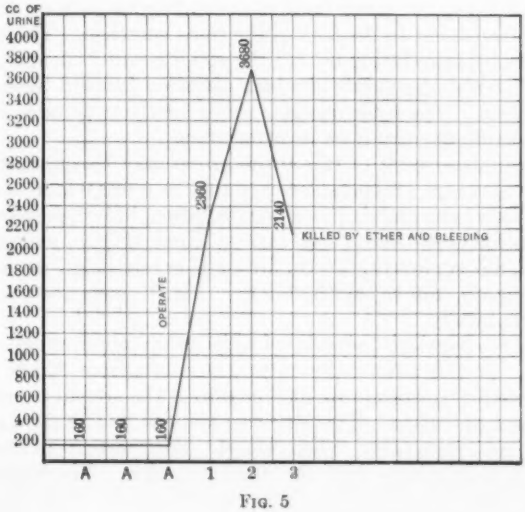

FIG. 5

Dog 28 was operated in the usual manner and in this instance also the gland was forced through the dural opening by the intracranial pressure. This herniation was not so marked as in the former case. Slight traction was made on the stalk, but an effort was made to avoid injury to the gland. The urine voided during the two days preceding operation measured 90 cc and 100 cc. During the first postoperative twenty-four hours 900 cc of urine were voided (Fig. 6). The quantity decreased to 200 cc during the second twenty-four hours. At this time this animal was in such bad condition that it was released from its cage. It died the following day. Postmortem examination showed no evidence of meningitis. The cause of death was bronchopneumonia. On the basis of these two observations a group of twenty dogs were operated.

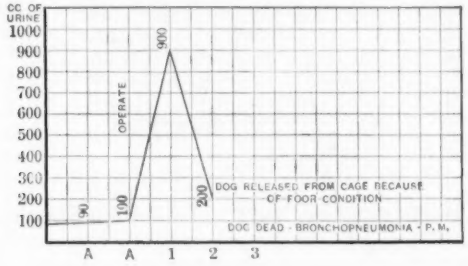

FIG. 6

Traction on the Stalk and Base of the Brain with as Little Injury to the Gland as Possible.—In these animals an effort was made to avoid trauma to the gland itself while making traction on the stalk and its attachment to the floor of the third ventricle. The traction was made by introducing behind the gland a pair of dental cotton-holding forceps, the points of which extended forward beneath the pars nervosa. The stalk was grasped as gently as possible and the traction made through it on its attachment.

The complete result of this entire group may be summarized as follows: Average preoperative excretion in twenty-four hours for the two days immediately preceding operation, 145 cc; postoperative excretion for each twenty-four hours: First, 893 cc; second, 1003 cc; third, 857 cc; fourth, 628 cc; fifth, 807 cc; sixth, 907 cc; seventh, 300 cc; eighth, 200 cc; ninth, 150 cc. Fig. 7 shows the composite result graphically.

The most marked polyuria of this group occurred in dog 55 (Fig. 8). In this animal the output increased from 200 cc on the days preceding operation to 4000 cc during the second twenty-four hours after operation. This dog was allowed to live six days and was in good condition when killed. Postmortem examination showed a hemorrhage into the third ventricle. The hypophysis

showed no gross changes other than a plastic exudate filling the defect in the sphenoid and covering the anterior lobe of the gland.

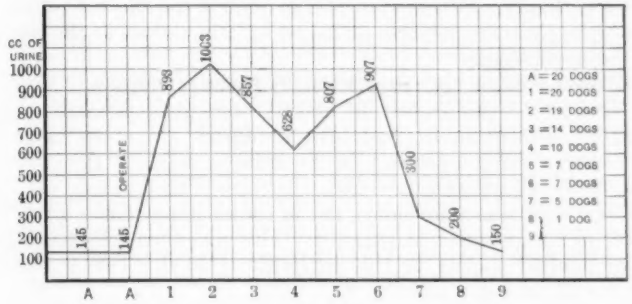

FIG. 7

It will be noted that the entire number of the dogs in this group were not allowed to survive the full period of their polyuria. It will also be observed that the average urinary excretion on the third, fourth and fifth days fell below the average for the second and the sixth day. This work was not for the study of the type and duration

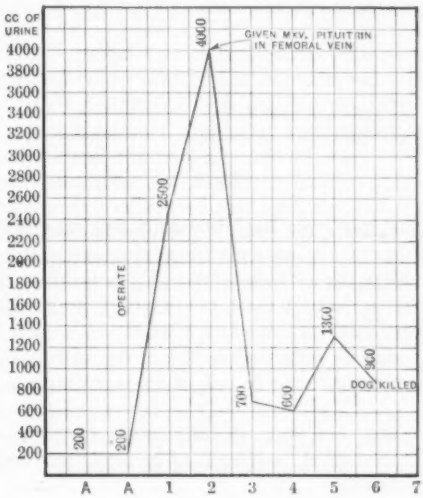

FIG. 8

of a polyuria induced by stimulation in the region of the hypophysis. Therefore, after the highest point in excretion had been reached,

or at least such a point as could be definitely regarded as a polyuria, many animals were used for supplementary experiments. Some were killed to secure tissue at the height of urinary excretion for cytologic study. Others were used to observe the effect of pituitrin and epinephrin on polyuria produced by stimulation in the region of the hypophysis.

Effect of Pituitrin upon Experimentally Produced Polyuria.—A group of six dogs (55, 56, 58, 59*a*, 63 and 64) were given pituitrin intravenously after polyuria had been produced. In every instance there was a marked decrease in the urine excretion in the twenty-four hours following the injection. In three of the animals (55, 59*a* and 63) there was a secondary rise in the excretory curve after the effect of the pituitrin had passed. This was then followed by a more gradual decline to the preoperative level. This is shown graphically in Fig. 4 and Fig. 8.

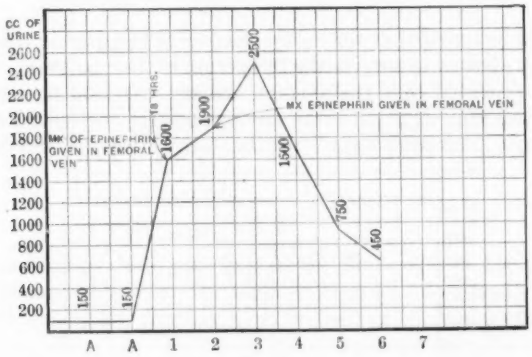

FIG. 9

Effect of Epinephrin upon Experimentally Produced Polyuria.—Five dogs (67, 69, 69*a* and 70) were given varying amounts of epinephrin intravenously after the establishment of a polyuria. Two of these dogs were given a second dose twenty-four hours after the first injection. In no instance was any change in the rate of excretion noted which could be regarded as the effect of the gland extract. In Fig. 9 the excretory rate in one of these animals is represented graphically.

Discussion.—The evidence dealing with the etiologic factors involved in the so-called "polyuria of hypophyseal origin" is conflicting and confusing.

That a polyuria is frequently associated with lesions in the sella turcica, involving to a greater or lesser degree the hypophysis, has been recognized clinically for many years. Hagenbach, in 1882, described a case of tuberculous meningitis—a caseous nodule in the infundibulum, dilated lateral and fourth ventricles—associated with

a marked polyuria, in a child aged four and a half years. Borelli, Meyenburghs, Haushalter and Lucien and others have reported similar processes, but with greater destruction of the gland. In one of Meyenburghs's cases only a small fragment of the anterior lobe remained.

Metastatic tumors in the pituitary gland associated with polyuria have been reported by M. Simmonds, H. Rosenhaupt, Sekiguchi, Kennaway and Mottram, Erdheim, Cushing, Fleckseder and others. In these cases the changes in the gland varied from a complete destruction to an involvement limited to the stalk alone (Cushing). In the 10 cases collected and reported by Simmonds, however, only 3 showed urinary increase. Of the remaining 7, 2 were described in some detail. In the first the pars nervosa, pars intermedia and infundibulum had been replaced by the tumor mass. In the second the entire gland, except a small part of the anterior lobe, had been destroyed by tumor. Neither of these cases was associated with any increase in urine excretion. Eason and Johnson and Strada and others describe similar cases in which the pars nervosa, pars intermedia and infundibulum are replaced completely or incompletely, in which no mention is made of polyuria.

A. Berge and Schulman have recently reported a case of diabetes insipidus which at postmortem examination showed gummatous lesions in the hypophysis, especially involving the pars nervosa. In this case the polyuria subsided temporarily when given extract of the posterior lobe.

E. Frank has reported a marked polyuria following the penetration and lodgment of a bullet in the sella turcica. He emphasizes the opinion that mechanical and thermal injury to the exposed gland may cause a long-continued polyuria, and concludes that this is due to the irritation of the pars intermedia.

The frequent association of diabetes insipidus with head injuries, especially fracture of the base of the skull, has been pointed out by Borszeky, Cushing, Kleeblath, Finkelnburg, Graham, Nothnagel and others, and has been attributed to injury of the pituitary gland. Cushing observed an "unaccountable postoperative polyuria of extreme grade" in a number of his surgically treated cases. In 1 case, a struma with moderate signs of hypopituitarism and a normal urinary output, there developed an extreme diabetes insipidus following a simple sellar decompression.

Polyuria has also been frequently noted associated with dwarfism, acromegalia and dystrophia adiposa genitalis, and upon roentgen-ray examination changes in the contour of the sella turcica have been noted.

Kahler, Bruns, Oppenheim, Ebstein, Pichler and others have recorded polyuria associated with various lesions of the base of the brain, including tumors of the third and fourth ventricles, the posterior perforated space and corpora mammillaria, syphilitic

processes in the region of the floor of the third ventricle, etc. In none of these cases, however, was involvement of the hypophysis excluded. Nor is it an easy matter to estimate the effect of such slight changes as occurred in the case of diabetes insipidus, reported by Götzel and Erdheim, in which the only variation in the hypophysis was a slight flattening as a result of pressure from a tumor of the third ventricle. Such a slight modification, as the cause of a marked polyuria, is difficult to reconcile, on a hypophyseal basis, with such cases as are reported by Cushing, in which, due to non-hypophyseal intrasellar tumors, the hypophysis is greatly flattened and distorted without change in the excretory rate.

From this very cursory review of the clinical aspect of this problem, though left in apparent confusion, it seems reasonable to conclude that:

1. Polyuria is not always associated with an increase in the activity of any part of the hypophysis, since it is seen with almost complete destruction of the gland.

2. Polyuria is not always associated with a decrease in the activity of any part of the gland, since almost complete destruction of the gland is seen without any change in the excretory rate.

Experimental work on polyuria dates from the classic work of Claude Bernard in 1849. He produced an increased urine excretion by injury to a point in the floor of the fourth ventricle anterior to his diabetic piqûre. Later, Eckhard verified Bernard's results and added several regions in the brain, stimulation of which produced polyuria. Kahler working on rabbits was able to produce a permanent polyuria closely resembling diabetes insipidus in man. By injecting small quantities of concentrated silver nitrate solution into various parts of the brain he was able to cause a polyuria accompanied by polydipsia, both lasting several weeks. The areas, injury to which were most likely to produce polyuria, were the corpus trapezoides of the pons and the lateral part of the exposed portion of the medulla. From the work of these investigators it would appear that a polyuria can be produced in dogs and rabbits by injury to the floor of the fourth ventricle, by lesions in the different parts of the middle lobe of the cerebellum and by injuries to the posterior part of the pons.

Of the more recent work that of Paulesco and Aschner stands out most prominently, as they first described and used successfully the two methods of exposure of the hypophysis which, with certain modifications, are the only two routes used at the present time. The transtemporal route of Paulesco, modified somewhat, is the method used by Cushing and his co-workers. Regardless of the operative procedure on the gland, the effect on urinary excretion in their various reports was inconstant. Polyuria was observed more frequently in those animals in which a silver clip was applied to the stalk and in subtotal removals with subcortical transplants than in any other groups. Homans, however, working on cats,

studying the effect of total removal and using the buccal route, observed polyuria in every instance. His method of removal of the gland was to grasp it by the stalk and pull it out. The removal was not complete in every instance, but in each case he produced a marked increase in the daily urinary output. Cushing also observed that the incidence of polyuria was greater in operated pups than in adult dogs. Though excellent in every particular of technic it seems quite possible that in all of this experimental work, one factor, though mentioned, was underestimated—that of traction upon and injury to the floor of the third ventricle. Due to the smaller available space in pups the lateral and upward displacement of the brain must be relatively much greater to gain an exposure equal or approaching that of a larger animal. It would produce a much greater amount of traction on the gland, stalk and its attachment.

The buccal or transsphenoidal method of approach of Aschner, which was the one used in this work, is also subject to certain objections. The certainty of a definite amount of infection, the danger of hemorrhage and the inaccurate estimation of stimulation or trauma inflicted to the gland and adjacent structures are the more important ones.

In this work it may be said only one animal showed any evidence of infection other than the slight plastic exudate over the exposed portion of the anterior lobe. In this case a cotton pack was inserted at the operation to fill the opening in the sphenoid bone. In all others the opening was left wide open and thus maintained free drainage into the mouth. By care we were able to avoid hemorrhage.

While it was impossible to regulate accurately the degree and extent of injury inflicted to the gland and its neighboring structures, we found no urinary increase of any consequence in any animal in which either the anterior or posterior lobes individually or the entire gland were stimulated by non-diffusible means, *i. e.*, heat or mechanical trauma. Stimulation of the hypophysis with an induced current produced polyuria. However, as an electric stimulus may be transmitted over a considerable distance it cannot be said that this trauma is limited to the gland itself or that the resulting urinary increase is of hypophyseal origin.

By traction on the stalk with an effort to avoid trauma to the gland itself we were able to produce polyuria regularly. We were able also to regulate roughly the degree of this increase—moderate or extreme—by modifying the amount of trauma (traction) exerted. Other animals operated, in which the same procedure was followed except for traction on the stalk, showed no or only slight polyuria. It will also be observed that in those experiments in which the hypophysis was mechanically stimulated the injury to the gland was greater than that inflicted in the process of making traction on the stalk. In the former the average daily preoperative output of

150 cc was increased to 297 cc in the first twenty-four hours and then gradually decreased, reaching normal in four days. In the latter the average daily preoperative excretion of 145 cc was increased to 893 cc in the first twenty-four hours and 1003 cc in second twenty-four hours after operation. It remained high and did not reach the preoperative level until the ninth day.

The three outstanding experiments to which we desire to call special attention are animals 2, 15 and 55. In the case of dog 2 the opening in the sphenoid was made so far posterior that the hypophysis was not exposed and the stimulation (cauterization) was applied to the region of the corpora mammillaria. In dog 15, due to peculiar anatomic arrangements, the gland came through the dural incision with considerable force, followed by a larger amount of cerebrospinal fluid than had been usually observed. Except for these variations there was nothing done which had on previous occasions produced more than a negligible increase in the urinary excretion. In dog 55 there was found at postmortem examination a hemorrhage into the third ventricle. This animal was operated in the series in which traction was made on the stalk and its attachment to the base of the brain. The associated polyuria was the most marked of the series.

In these three animals we see, in addition to a conspicuous increase in the urinary output, evidence of what quite possibly is the active etiologic factor. In dogs 2 and 55 there was gross evidence of injury to the base of the brain (the region of the floor of the third ventricle). In animal 15 the force with which the gland herniated through the dural opening may be considered to have produced trauma of the same sort, but not appreciable macroscopically. This is in accord with the results of Camus and Roussy, published in 1914.

Conclusions.—1. Clinical evidence, though indefinite, indicates that neither increased nor decreased activity of any portion of the hypophysis is uniformly associated with polyuria.

2. Experimental lesions of the hypophysis itself are not constant in the production of polyuria. Some additional element is the determining factor.

3. Experimental lesions of the hypophysis, similar to those producing negligible excretory changes, when associated with traction upon its attachment to the floor of the third ventricle uniformly produced polyuria. The degree of polyuria was roughly in proportion to the amount of traction.

4. Polyuria associated with hypophyseal changes is due to stimulation of the regional base of the brain, floor of the ventricle, corpora mammillaria, etc.

5. Intravenous injections of pituitrin temporarily lowered the excretory rate in a polyuria thus produced.

6. Intravenous injections of epinephrin have no effect on polyuria of this type in dogs.

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THE CORRELATION OF CLINICAL AND PATHOLOGICAL FINDINGS IN NEPHRITIS.

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The idea that clinical findings in nephritis and laboratory results do not agree, and that the lesion in the kidney cannot be interpreted in terms of function, has been long current among physicians. This mental attitude toward the problem is quite generally, if unconsciously, assumed at the bedside and undoubtedly does harm on

the whole by tending to make the management of individual cases too much of a group matter without due regard to evaluating, as far as possible, the function of each part of the kidney mechanism and treating the particular patient accordingly.

Widely different clinical manifestations are grouped together as nephritis, or some substitute term, such as nephrosis or nephropathy, is used. The child, who during an attack of scarlet fever becomes dropsical, passes a small amount of urine of high specific gravity, rich in albumin and casts, without retention of nitrogen in the blood, and with perhaps little increase of blood-pressure, is said to have "nephritis." At the other extreme of the series we find the man past middle life who has no anasarca, who passes abundant urine of low specific gravity, with perhaps the faintest trace of albumin and a few hyaline casts, and who presents marked signs of nitrogen retention and increased blood-pressure.

We know that these two conditions, and many others with varying clinical pictures lying between these two extremes, are due to disturbances of kidney function which result from injury to the kidney and its attendant reactions of repair. We do not know, in most cases, exactly what caused the injury and are prevented by lack of this knowledge from classifying them etiologically.

Two entirely redundant, and for the most part meaningless, terms have crept into the literature. These are "nephropathy" and "nephrosis." The latter has no etymological excuse for existence and the former means "any disease of the kidney." The words nephropathy and nephrosis have been used by most writers to designate injury to the kidney without attendant inflammatory reaction, or injury to the kidney, with consequent fibrous change, without an acute inflammatory stage, as evidenced by exudate, and migration of cellular elements. If it were generally agreed among pathologists that only those processes attended by exudate and round-cell infiltration should be termed inflammations the above words might be used as substitutes. It seems better to the author not to tamper with our present conception of the nature of the inflammatory process and to consider the matter from a broad biological point of view.

Any living tissue when injured by any agency whatsoever is subject to a series of phenomena which have as their basic biological purpose the repair of the injury. These changes, taken together, no matter in what stage of the process they are observed, constitute inflammation (Adami, Warthin).

We can conceive that we may view the tissue so soon after the injury that we cannot detect any reaction by our usual methods of examination, or we may view the tissue so long after the reaction is complete that we see only the scars left behind by the attempts at healing. There is no sharp line of demarcation between any of these stages, and different noxa are reacted to in quite different ways;

therefore it is quite academic, as well as wholly impracticable, to split off "nephroses" and nephropathies" in our classification and separate them from the "nephritides."

The kidney may be considered, for purposes of study, as consisting of a glomerulus with a system of tubules and their attendant blood supply.

The primitive metazoa lived in the sea and had a very simple problem of excretion presented to them. These animals had an abundant supply of water and salts at their command at all times. They could filter through their primitive segmental nephridia several times their weight of water in twenty-four hours and needed no mechanism for the conservation of salt. Therefore, there was developed in them the simplest kind of a filter by which the catabolites, resulting from their life processes were diffused into the surrounding sea from their celomic cavities. This primitive filter is the analogue of the glomerulus which later becomes attached to or rather invaded by a vascular tuft; but the glomerulus retains down to man himself the primitive function of a simple filter and nothing more.

The next problem which was presented to the kidney mechanism resulted when the marine animal became a fresh-water animal or fresh-water amphibian. In these cases water was still present in abundance, and more than the animal's weight in urine could be secreted in twenty-four hours; but the valuable salts were no longer present in the liquid and had to be conserved. Thus the kidney tubule was developed, primarily, as a mechanism to conserve salt and resorb these radicals as the glomerular filtrate passed on its way to the excretory opening.

As animals became more terrestrial in their habits a new necessity arrived in the shape of a demand for water conservation. It was no longer expedient to drink the large amount of water necessary to dispose of catabolites through a simple filter. In the case of the human animal it would be necessary to drink a wholly impractical amount of water if the catabolites were to be removed as simple filtrates through the glomerular mechanism. An example makes this clear. There are 30 mg. of urea in 100 cc of blood, or 0.3 gram per liter. In order to get rid of 20 grams of urea in twenty-four hours, 67 liters of water would have to be filtered through the glomeruli. In order to pass 67 liters of urine the animal would have to drink at least that much water, which would again amount to as much as the individual's weight.

Before the vertebrate stage evolution had already developed the tubular mechanism for resorbing such salts as were necessary from the glomerular filtrate, and to this function of the tubule the function of resorption of water was added. By resorption of water by the tubules as the glomerular filtrate passed to the exterior the animal might use his water over and over again and avoid drinking

or passing in the urine such excessive quantities; but still the filtration through the glomerulus of such large quantities of fluid would be a wasteful process requiring the specific and selective resorptive function on the part of the tubule of a very large quantity of material. Thus the last and most important function of the tubule was developed—namely, the function of actively secreting waste nitrogen. This allowed the quantity of glomerular filtrate to be cut down remarkably, and the mammalian kidney tubule as found at the present stage of development performs a threefold function, which functions have probably been imposed upon it in the course of evolution in the following order:

1. Selective resorption of salts.
2. Resorption of water with resulting concentration of the urine.
3. Active secretion of waste nitrogen (urea, uric acid).

The glomerulus as above stated acts as a simple filter and probably filters in the neighborhood of 6 liters of water into the tubular mechanism each twenty-four hours. Of this 6 liters the tubules usually resorb about $4\frac{1}{2}$ to 5 liters. The urine is thereby concentrated and the salts necessary to the organism are selectively resorbed. While the glomerular filtrate is passing down the tubule the waste nitrogen (urea, uric acid) is secreted by the tubule into the lumen and added to the glomerular filtrate.[1]

In general it may be said, then that the secretion of water and salts depends upon glomerular function and the ability of the kidney to concentrate the urine, to conserve necessary salt radicals and to eliminate nitrogen depends upon the tubule function. We should therefore expect to find, when considered from a functional point of view, four main groups of nephritics:

1. Diffuse glomerular injury preponderating.
2. Diffuse tubular injury preponderating.
3. Focal (spotted) embolic lesions producing acute inflammatory reaction in circumscribed areas, with the majority of the kidney cortex free to carry on function.
4. Diffuse fibrous kidney, which by reason of arteriosclerosis or of some other slowly acting unknown cause has destroyed both glomeruli and tubules to an extent such as to embarrass function. This class is made up of the so-called cases of interstitial nephritis and late stages of Group 3.

The author does not claim that each of these groups is always clear cut, and distinctly separate from the others, but believes that almost pure examples of each type are readily found if looked for. Further, when in acute cases death occurs before secondary and additional injury sets in from complicating factors the lesion found microscopically usually is the one expected, if the symptoms and

[1] For a full discussion of the mechanism of kidney secretion, including the literature, see Baylis, W. M. (Principles of General Pathology, Longmans Green & Co., 1915) and Cushny, A. R. (The Secretion of Urine, Longmans, Green & Co., 1917).

signs have been interpreted in the light of the functional mechanism above set forth.

The following examples illustrate each group:

1. Acute Diffuse Glomerular Injury.

If our present belief that the glomerulus is a simple filter, having primarily to do with elimination of water and salt is correct, we should expect that any noxa injuring the glomeruli diffusely, but leaving the tubule relatively uninvolved, would have the following effect:

(*a*) The quantity of urine and the salt output would be decreased.

(*b*) There would be salt and water retention with general anasarca.

(*c*) The nitrogen elimination would go on uninterrupted as long as there was sufficient urine secreted to wash it down the tubules. This would be the case as long as the glomerular injury was purely or for the most part capsular; but if the vascular tufts became thrombosed or blocked off by the pressure of capsular exudate then the tubules would be deprived of blood supply and would partake of the injury.

(*d*) The injury to the glomerulus allows the escape of large quantities of albumin.

The clinical manifestations which we should expect of an acute nephritic with a pure glomerular injury are as follows:

(*a*) General anasarca with chloride retention without high blood nitrogen.

(*b*) Small amount of urine in twenty-four hours, of high specific gravity and abundant albumin and casts.

(*c*) A blood-pressure which becomes progressively elevated as the glomerular function fails and falls as soon as the glomerular function is reëstablished.

A photomicrograph of the lesion in the kidney from such a case is appended (Fig. 1). It will be noticed that the glomerular capsule is filled with a cellular exudate and that the tubular system is apparently uninjured.

The question of the management of these cases is an important one. The indications to be met are the low urinary output, the anasarca and the marked albumin loss. These patients develop a severe anemia rather rapidly, probably due to the albumin loss. The loss of large quantities of albumin with consequent lowering of the colloidal pressure of the serum and a relative hydremia has never been sufficiently investigated as a cause contributing to the anasarca of nephritis. The pure or nearly pure glomerular type of diffuse nephritis—that is, the type with high albumin loss without nitrogen retention in the blood—is the one in which the best results are to be expected from Epstein's high protein feeding.

As to whether salt is primarily and specifically retained, or whether it is merely retained because water cannot filter through the glomerular membrane, is still unsettled. Most authorities believe that

salt is retained primarily and edema develops in nephritis because of salt retention in the tissue. The evidence in support of this idea is entirely insufficient for it to be considered proved or even presumptively established. As a matter of fact, in the vast majority of cases water and salt are retained together, and for the same reason—namely, that the filter is clogged. The salt is not excreted because the water is not excreted, and when the kidney becomes capable of eliminating water, salt is no longer retained.

The disciples of the primary salt retention doctrine point out that if salt be removed from the dietary the patient looses his edema. When this is the case (and everyone knows that often edema, demon-

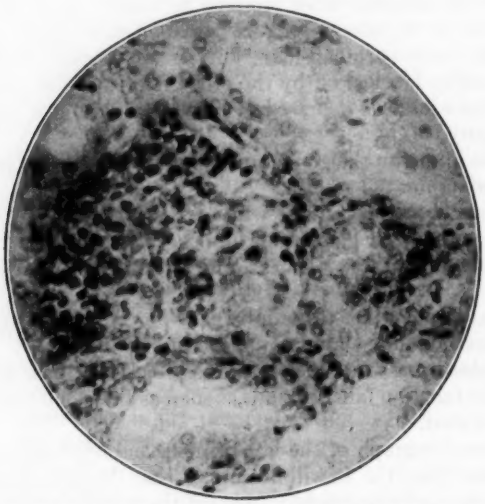

FIG. 1.—Acute glomerular nephritis. Capsular space filled with exudate. Tubules relatively normal.

strably nephritic and not cardiac in origin, remains in spite of the removal of salt from the dietary) it is due to two and possibly more factors. The first of these is that any edematous patient when deprived of salt automatically drinks a minimum amount of fluid. The writer has repeatedly verified this point by observation of the fluid intake without the patient's knowledge or any suggestion regarding the amount of water taken. The balance in this way is often restored and the kidney is able to gradually gain on the edema. It is also quite well known that there is a wide difference in the facility with which electrolytes pass through colloidal membranes and an injured glomerulus may well have its permeability to sodium chloride lowered without water permeability being seriously inter-

fered with. Of course, this latter explanation is simply the primary salt retention notion in another form.

For a certain small percentage of cases with edema it seems as though such a hypothesis must be entertained because we occasionally see patients with nephritis associated with edema who will get rid of their anasarca as soon as we restrict salt in spite of the fact that fluid intake is kept up even as high in some cases as 1800 cc in twenty-four hours.

2. Acute Diffuse Tubular Injury.

If the tubular epithelium were uniformly and diffusely injured, leaving the glomeruli and blood supply intact, we should expect glomerular function to be preserved and tubular function to be

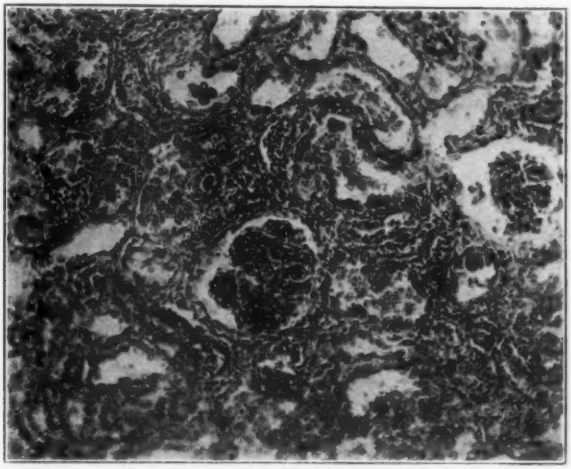

FIG. 2.—Mercuric chloride poisoning. Tubule injury of moderately severe degree.

interfered with proportionately to the degree of injury. In this case we shall expect:

(*a*) Normal (or increased) urinary output without salt retention or edema.

(*b*) Urine of normal or low specific gravity with a varying amount of albumin depending on the degree of the injury.

(*c*) Retention of urea, uric acid and finally creatinine with or without so-called uremic manifestations, such as gradually deepening confusion, coma or convulsive seizures.

The best examples of this type are the cases of mercuric chloride poisoning, two of which with different degrees of injury are shown in the appended photomicrographs (Figs. 2 and 3).

Neither of these patients developed anasarca. The total salt and fluid output remained normal. The sediment contained many epi-

thelial and granular casts. There was a progressive rise of the blood nitrogen until death. Another patient with mercuric chloride poisoning, who recovered, secreted from 1200 to 1700 cc of urine throughout her stay in the hospital, although the total non-coagulable nitrogen rose to 237 mg., and she was delirious for several days. The salt output was normal and no anasarca developed.

The incidences illustrate very well the effects of a diffuse tubular injury, rapidly produced, without glomerular involvement.

The relation of tubular injury to so-called uremia is of interest, but incapable of fruitful discussion at present. It is a fact that cases clinically "uremia" have anatomical evidence of tubular injury and have the blood chemical findings of depressed tubule function. On the other hand it is well known that absolute inhibition of kidney

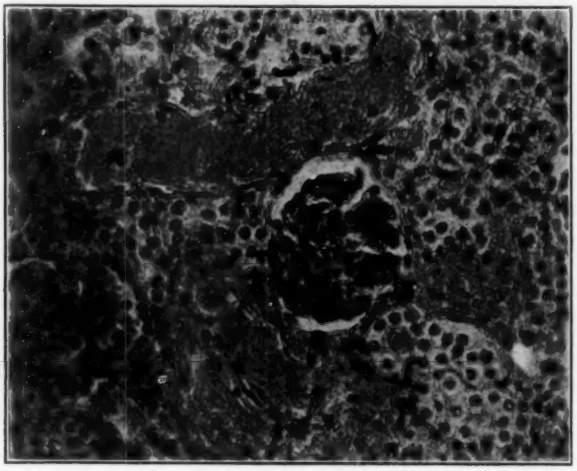

FIG. 3.—Mercuric chloride poisoning. Complete destruction of tubular epithelium; coagulation necrosis.

function, such as obstruction of both ureters, is not clinically attended by uremic manifestations, although the blood chemical findings point to a complete retention of substances secreted by the tubules. Some authors (Foster) have attempted to show that "convulsive" uremia differs from the ordinary type in that methyl guanidine or related substances are found in the urine, and it has been suggested that the convulsions have been due to the presence of these substances. The assumption is of the *post hoc propter hoc* variety, and before it is assumed that the convulsions are due to methyl guanidine or its congeners it should be recalled that creatine and creatinine, which are derivatives of methyl guanidine, are substances closely related to muscle catabolism, and the above-mentioned bases may be rather the result of the convulsions than their

cause. The author believes that the manifestations grouped together clinically under the head of uremia are the result of brain edema of varying degrees and distribution, and that nitrogen retention and uremia, while clinically coincident, are not necessarily etiologically related. In this connection it is of interest to recall Martin Fisher's belief that amines may cause edema as well as acids and alkalis. The view that uremia is related to brain edema is one of the earliest that was offered. Ludwig Traube, in 1848, so explained it, and the idea has recently been revived. In the author's experience with a large autopsy material, wet brain is the most constant autopsy finding in patients dying of "uremia." Some time ago we pointed out the importance of estimating the preformed ammonia in the spinal fluid of these patients.

The occurrence of acute diffuse glomerular nephritis and acute diffuse tubular nephritis as distinct clinical entities is not uncommon. The glomerular type occurs oftener than the pure tubular, and still more often a glomerular injury progresses until the tubule partakes of the damage and we have functional evidence of a true diffuse nephritis with both glomerular and tubular malfunction. The best example of tubular injury is found in acute mercuric chloride poisoning. Here the continued normal output of water and chlorides, with marked retention of nitrogen and "uremic symptoms," taken with the postmortem findings, as shown in the photomicrographs, make a clear case of tubule injury. We also meet with certain cases of the kidney of pregnancy which appear to have primarily a tubular injury usually coupled with exacerbations of true diffuse nephritis with accompanying glomerular injury.

3. Embolic or "Focal" Injury.

The third group is most interesting and embraces a large number of the cases of so-called "acute nephritis" or "recurrent acute nephritis" and "subacute chronic parenchymatous nephritis." These are the cases which result from multiple embolic involvement from focal infection elsewhere in the body. The photomicrographs from two cases of this type, one recent and acute and one of longer duration, are shown in Figs. 4 and 5. The nature of the lesions here makes it plain that areas of intense inflammation and tissue destruction are simply distributed in a spotted fashion throughout an otherwise normal cortex.

These cases in their early stages are characterized by the fact that they show marked evidence of kidney lesion, as judged by albumin and casts and even blood in the urine; but their kidney function, judged by blood chemistry, urinary output, salt elimination and blood-pressure, is normal or quickly becomes normal after the first few days in bed. The explanation of these findings is, of course, evident in that we have ample normal kidney parenchyma functioning in between the involved areas. The products of the inflammatory reaction and the results of the injury, albumin, casts

and blood are found in the urine. These come down from the involved areas. The rest of the kidney is normal and functions

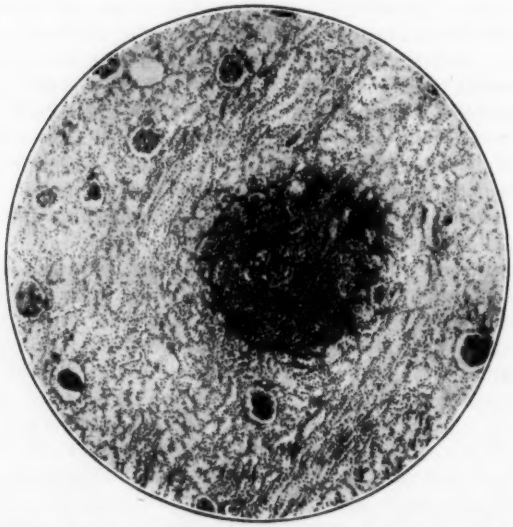

FIG. 4.—Embolic (focal) nephritis. Recent lesion. Area of acute inflammatory reaction surrounded by normal kidney tissue.

FIG. 5.—Focal nephritis. Recent (subacute) lesion in the course of a chronic embolic nephritis.

normally so that we do not find nitrogen, water or salt retention; and high blood-pressure does not supervene until late, when so much parenchyma has been destroyed piecemeal as to leave insufficient cortex to perform normal function.

These cases are subject to acute recrudescence usually at times of exacerbations of their focal infections. At these times they may present signs of temporary embarrassment of kidney function. Usually this takes the form of mild localized edemas and moderate salt retention; sometimes, though quite rarely, of lowered urinary output and mild nitrogen retention. These signs soon disappear upon putting the patient to bed and instituting dietary restrictions, leaving behind the albumin and casts and evidence of focal involvement. These exacerbations with edema and low output, and usually also moderate nitrogen retention, are possibly due to the attendant edema of the kidney, incident to a recent shower of bacterial emboli and the acute inflammatory reaction resulting. This clears up, leaving the focal areas of infiltration with normal kidney parenchyma in between.

The subsequent course of these cases is interesting. In the author's opinion the majority of cases of so-called chronic parenchymatous nephritis come to us through this focal involvement route. Gradually the kidney parenchyma is replaced by scar tissue until we have the irregularly coarse granular kidney classically known as the secondary contracted. As time goes on, and progressively more and more of the kidney cortex is replaced by scar tissue, the periods of anasarca and low output come more frequently and the nitrogen gradually rises as well as the blood-pressure. Finally, we have at the terminal stage the classical clinical picture of chronic parenchymatous nephritis.

The management of these cases must be guided by the amount of functional injury. They develop anemia easily and must not be allowed to suffer from albumin want, since they loose albumin continuously and sometimes in large quantities in the urine. The removal of the focal infection, if accomplished early after the first or at most the second exacerbation, is attended with good results in the majority of cases. Those due to tonsils have the best prognosis. Those where the primary focus is apparently the nasal sinuses do not seem to answer so promptly to surgical treatment of the focus, and in the older cases with frequent exacerbations and even slight evidence of beginning malfunction of the kidney practically nothing is accomplished so far as the kidney is concerned by treating the primary focus.

4. Nephritis Due to Vascular Degeneration.

The fourth group comprises those cases usually designated clinically as chronic interstitial nephritis. There is a diffuse fibrosis of the kidney, as a whole, attended by marked arteriosclerosis and arteriolar thickening. Formerly it was the custom to distinguish

between true interstitial nephritis and chronic "vascular" kidney, but this distinction will not hold either clinically or pathologically. The interesting diffuse changes produced by Newburgh by feeding diets high in protein are of this diffuse interstitial type, and the changes found in the kidney are possibly even here of vascular origin. Ever since the early work of Johnson and Gull and Sutton the importance of which was later emphasized by Jores, the kidney of chronic interstitial nephritis, has been gradually recognized as a part of a general vascular disease. Moscowitz has recently reëmphasized the relation of this type of nephritis to generalized arteriosclerosis. The mechanism of the malfunction is in this group most interesting, because, the writer believes, the high blood-pressure in this group is unrelated to the kidney etiologically and is entirely due to the primary arteriosclerosis. It is easy to visualize the pathogenesis of the lesion by examining a series of sections from cases in various stages. We first have the diffuse arteriolar degeneration with thickening of the arteriole walls and lowering of the blood volume delivered to the part in unit time; further, the capacity of the vessels to dilate and contract under different stimuli is lowered. This is a more or less diffuse phenomenon throughout the body. Sometimes the brain is more intensely involved early and we get the clinical manifestations of cerebral arteriosclerosis, or it may be the spinal cord, the pancreas or some other organ is first embarrassed by want of an adequate and variable blood supply by reason of thickened vessels. In many of these cases the kidney escapes completely until apoplexy or some cardiac accident ends the scene. The kidney is, however, frequently involved in the process and partakes of the injury. The point to be kept in mind is that not the kidney but the vascular system is the organ primarily diseased.

During the progression of the arteriosclerosis the blood-pressure has been constantly rising to meet the demands of the tissues for blood. If at this stage we find no kidney malfunction and no urinary evidence of parenchymal injury we are accustomed to use Sir Clifford Albutt's term and say that we are dealing with a case of hyperpiesis. These are the cases in which the kidney has been relatively spared in the general process. If the kidney has not been spared the parenchyma gradually undergoes fibrosis diffusely, the scar tissue becoming hyaline and contracting until we have the very small, finely granular, "primary contracted kidney." At this stage the tubules and glomeruli find themselves diffusely and uniformly killed off until only a number insufficient for function under ordinary conditions are left. But all this time *the blood-pressure has been gradually rising*, due to the arteriosclerosis and not to the kidney injury. *This high blood-pressure allows the few glomeruli to do the work of the many*, and obeying the first law of kidney secretion, the high blood-pressure filters enough fluid through the few glomeruli that are left to keep up the quantity output and chloride elimina-

tion to normal. Anyone who doubts that this is the mechanism has but to observe the behavior of these cases during a cardiac decompensation to be convinced.

The injured glomeruli then are compensated for by the high blood-pressure, keeping the urinary and chloride output up to normal during cardiac efficiency; *but there is nothing to compensate for the injured tubules.* On this account nitrogen retention supervenes and the patient loses his power to concentrate the urine properly because of loss of resorptive power on the part of the tubule. The classical signs of the so-called interstitial nephritis thus can be deduced from the type of injury:

(*a*) High blood-pressure.

(*b*) Normal or increased urinary output without salt retention due to the filtration by the high blood-pressure of sufficient fluid through fewer glomeruli than are required under normal conditions.

(*c*) Urine of low specific gravity and low total solids because the injured tubules are unable to concentrate the urine as well as under normal conditions.

(*d*) Small trace of albumin and hyaline casts resulting from this type of injury.

(*e*) Uric acid, urea and creatinine retention because of uncompensated tubular injury.

Many interesting questions arise besides the ones mentioned. It is a question whether the salt hunger manifested by these patients is not really due to salt loss because of inability of the kidney tubule to properly conserve it. In the writer's mind no adequate grounds exist for the restriction on salt often put upon this class of patient.

Clinicians have long ago learned not to try to reduce the blood-pressure in these cases and the importance of the blood-pressure in maintaining the efficiency of the glomerular filters is instantly manifested during myocardial breakdown. Therapeutically the maintenance of the cardiac efficiency and the reduction of the blood nitrogen to the lowest possible level are the major indications. The uremias that supervene require special management not within the scope of this paper. We have a right to expect the best results in those cases detected early. There is some difference of opinion as to just what are the earliest signs of kidney involvement in these cases of hyperpiesis. Probably no one criterion will be discovered to cover all the cases. Newburgh's work suggests that restriction of protein food might be indicated whenever the blood-pressure is abnormally high regardless of laboratory signs of lowered kidney function. The rise in the uric acid level to 3.5 mg. or higher per 100 cc of blood is quite a constant finding in hyperpietics and probably indicates definitely lowered kidney function. The next sign usually found is an increase in the night urine associated with a delayed meal stimulus and a tendency to fixation of the specific gravity at a low level. This urinary data should be gathered in the

manner suggested by Mosenthal with the patient on the standard diet. The writer prefers to keep the patient on the diet for two days and collect the data during the second twenty-four-hour period.

The clinician now always has the means at hand to collect data from which he can evaluate separately the various functions of the kidney and from them reason back to the lesion. More important than this, the patient's dietary regimen may be made to fit his ability to eliminate, and unnecessary restrictions of protein, water and salt can be avoided.

LOWERED VITAL CAPACITY OF THE LUNGS IN A CASE OF PRIMARY HEPATIC TUMOR WITH PULMONARY METASTASES.

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The following case, which came under observation in the medical ward of the Peter Bent Brigham Hospital, illustrates a condition of considerable rarity and presents several features of clinical as well as pathological interest.

The patient, an unmarried seamstress, aged sixty years, first was seen in the outdoor department of the Peter Bent Brigham Hospital (P. B. B. H., O. D. D., No. 59170) October 2, 1919, where she came complaining of pain and stiffness in both knees of fourteen years' duration, accentuated by motion. She was still able to get about unaided except for the occasional use of a cane. An incidental complaint was that of occasional colicky pains over the upper abdomen, radiating into the back, of ten years' duration, never accompanied by jaundice, occurring most often at night, with rare vomiting. Physical examination at that time showed a blood-pressure of 230 systolic and 124 diastolic, with a coincident mild cardiac hypertrophy, and a soft-blowing systolic murmur not transmitted to the axilla. The knees presented a slight boggy, periarticular swelling, with some pain on manipulation. Lungs, abdomen and the remainder of the examination were reported negative. The urine was normal. She was given potassium iodide and put on a low protein, salt-poor diet. Roentgenograms of both knee-joints were taken which showed definite hypertrophic arthritic changes involving the spine and tuberosities of the tibiæ and condyles of the femurs. Throughout that month and the next, she continued under this regimen, with the addition of baking and massage, and reported some improvement in her knees. Only on one occasion did she complain

of a slight cough, which promptly subsided. Two and a half months later she had developed tiredness, palpitation and a slight dyspnea on exertion, which apparently were taken as manifestations of her cardiovascular condition, and nitroglycerin, .06 mg., t. i. d., was prescribed, with subsequent improvement, though she continued to fatigue easily.

Thereafter her course was uneventful, until August 25, 1920, when she returned with her former complaints, and in addition mentioned that she had been expectorating small amounts of blood-streaked sputum occasionally at night. Flat and stereoscopic roentgenograms of the chest (Fig. 1) were taken with the following report: "The chest is symmetrical with a normal diaphragm, which

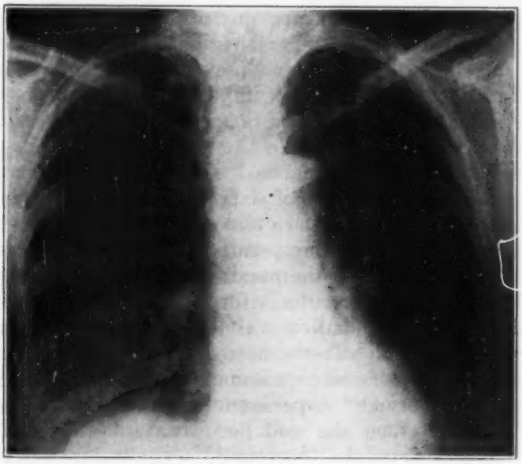

FIG. 1.—Roentgenogram of the chest, taken August 27, showing marked increased infiltration about the roots of both lungs, and metastases into the lung fields themselves, the latter being more numberous in the lower lobes, though the original plates show a definite upper lobe metastasis as well.

moves freely during respiration. The trachea is in the midline. There is a marked increase in the density of the root shadows, especially on the right side, which definitely shows glandular enlargement. There is a bilateral 'spotty' consolidation throughout both lungs, most marked in the lower lobes. This consolidation has every appearance of being metastatic malignancy and not tuberculosis." Barium studies of the gastro-intestinal tract, instituted thereafter in search of a primary source, were entirely negative, and as the patient was commencing to have more copious hemoptyses, she was sent into the hospital on September 16.

An additional and more complete history relative to her pulmonary condition gave a present illness of one month's duration, the

chief symptoms of which were an increasing sense of "tightness" in the chest, some "wheezing" on breathing, progressing dyspnea, occasional slight hemoptyses and insomnia. With these were associated increasing weakness and a loss in weight of about twenty pounds.

Family History. Her father and both paternal grandparents had died in middle age of tuberculosis. Her mother died at forty-seven of "shock."

Marital History. The patient was single and of abstemious habits. She had always lived in Boston or vicinity.

Past History. Measles at six, "intermittent fever" at sixteen, and malaria at forty-six were her only acute infections. Following vague pelvic symptoms she was operated upon about ten years ago and double oöphorectomy and hysterectomy were performed, and she was told that gall-stones were found in the gall-bladder, but that her condition prevented further investigation. Otherwise, there was nothing of importance in her history, except for a long-standing nocturia and the previously mentioned arthritis in the knees.

Physical Examination. Showed a well-developed and rather undernourished adult female of sixty-one years, lying comfortably in bed without pain or dyspnea and mentally coöperative. Skull, scalp, hair, face and skin were negative. Eyes were normal except for a slight irregularity of the pupils and a temporal hemianopsia, probably explained by a partially formed cataract in the right eye. Ophthalmoscopic examination was negative. Ears, nose, mouth and lips were normal. Teeth showed a few of the upper incisors remaining; the lowers were missing. Tongue, tonsils, pharynx and neck were normal. A persistent huskiness was noted in the patient's voice, which she said had always been present. The thorax was symmetrical and expanded equally on both sides; no abnormalities were noted. The heart showed the left border of dulness 10 cm. from the midsternal line and the right border of dulness at the right sternal margin; the supracardiac dulness was not increased. Sounds were regular and of good quality, and there was a soft-blowing systolic murmur best heard at the apex. Pulmonary and aortic second sounds were somewhat accentuated. The vessels were relatively normal. Blood-pressure: systolic, 180; diastolic 90. Lungs, tactile and vocal fremitus were well transmitted and breath sounds were bronchovesicular throughout both lungs. Percussion showed questionable small areas of dulness posteriorly, most marked in the region of the hila. Fine crepitant rales were heard throughout the left lung and there were a few fine moist rales at the right base behind and over the right lower chest anteriorly. The right border of the diaphragm was higher than the left and expansion of the bases was only fair. The abdomen was reported negative, except for the epigastrium and right hypo-

chrondrium, over which there was an increased resistance to palpation, with the sensation of an underlying mass, the character of which, however, could not be determined on account of the rigidity of the abdominal musculature. Since the liver dulness extended from the sixth rib above to three finger-breadths below the costal margin it was felt that there was an enlargement of that organ. Gall-bladder, spleen and kidneys were not palpable. There was no peripheral adenopathy and the bones and extremities were not remarkable. Vaginal and rectal examinations revealed no pathology, except that the fundus uteri could not be felt.

Clinical Course of the Disease. Subsequent examinations by various members of the house and visiting staff bore out the entrance physical findings. However, as palpation of the mass in the right upper quadrant was so unsatisfactory and enlargement of the right kidney could not be ruled out, pyelograms and cystoscopic studies were suggested for this purpose. The latter showed no evidence of genito-urinary lesions and the former demonstrated both kidneys in normal position with normal pelves and calices. Incidentally multiple gall-stone shadows were seen overlying the right kidney shadow and there was a distinct sacralization of the fifth lumbar vertebra.

Subjectively, for the succeeding three weeks, the patient's condition changed very little, except for a gradually increasing weakness. She continued to expectorate varying amounts of a more or less blood-streaked sputum, and although during the first ten days she lost about six pounds in weight, in the following week she regained one and one-half pounds. The number and location of rales heard over both chests varied considerably from one examination to the next, but breath sounds over the left lung had become distinctly cog-wheel in character.

A note by Dr. Henry A. Christian on October 7 follows: "The epigastrium down to a point two fingers above the navel is elevated by a mass which moves distinctly with respiration. It has a fairly distinct lower rounded border. It can be traced across the abdomen from the left costal margin in the anterior axillary line to the right flank at the level of the anterior-superior spine of the ileum. The mass is firm. The surface is smooth. It seems to be an enlarged liver. The gall-bladder cannot be felt."

Further roentgen-ray examination of the chest at this time (Fig. 2) showed the condition there to be considerably more advanced than before, with increased density of the glands about the left hilum.

From this point the patient's condition became progressively worse. On October 18 she complained of loss of appetite, which to that point had been sustained, and of a sensation of "choking up" in the chest, with expectoration of larger quantities of blood. There were now numerous crepitant rales throughout both lungs, moist

rales at the bases and friction rubs in either axilla. The liver enlargement remained as noted above. By October 27 insomnia became a prominent symptom, chest pain and respiratory difficulty were much more marked and the voice became increasingly husky, for which laryngoscopic examination revealed no cause. Repeated vaginal and rectal examinations had continued negative and other signs were as above. Thereafter the various factors increased in intensity, and the patient died, apparently of respiratory failure, at 1.30 A.M., November 1, her forty-seventh day in the hospital.

Temperature. The morning temperature varied from 96.8° to 99°, averaging 98°, while the evening temperature varied from 98° to 100.2° averaging slightly over 99°.

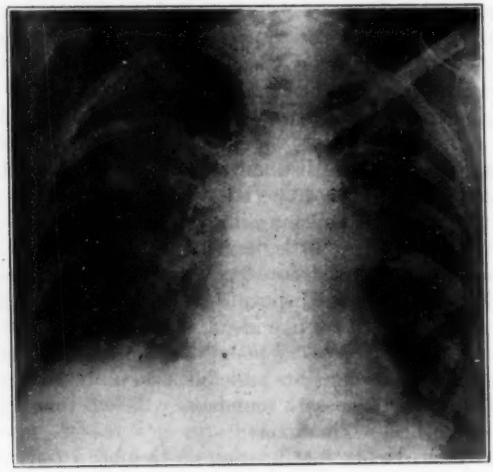

FIG. 2.—Taken October 7, showing the metastases much more numerous, and the root infiltration more extensive than on the first plate.

Pulse averaged 90 until the last ten days in the hospital, after which it underwent a steady increase, reaching 130 on the four days preceding exodus.

Respiration remained at 20 per minute until one week preceding death, at which point it suddenly rose to 35 and remained between 30 and 40 until the end.

Weight fell steadily but for one transient rise, from 63.6 kg. at entrance to 58.3 kg. one week before exit.

Blood-pressure. Weekly determinations showed systolic readings varying from 180 to 200 during the first two weeks and from 158 to 174 in the last five weeks, and diastolic from 90 to 110 during the first period and from 70 to 90 in the latter.

Vital Capacity of the Lungs. As compared with a normal of 3120 cc for a person of the patient's sex, age, height and weight her vital capacity was 1200 cc (41.5 per cent) five days after entry, rose to 1300 cc at the end of three weeks and fell to 800 cc ten days before death. From that time on her bodily discomfort was too great to permit of further trials.

Clinical Pathology. (*a*) Blood Wassermann negative.

(*b*) Phenolsulphonephthalein output normal.

(*c*) Gastric analysis showed a normal acidity curve. Benzidine test for occult blood was negative in all specimens and microscopical examination revealed no abnormalities.

(*d*) Sputum examinations, made at least bi-weekly, showed almost routinely a frothy, watery material, streaked with fresh blood and a stringy mucopurulent substance. Careful search for tubercle bacilli or bits of tumor tissue were consistently without positive results; organisms were present in moderate numbers, the predominating type being Gram-positive cocci, arranged in pairs and chains of varying lengths.

(*e*) Stool examination was constantly negative.

(*f*) Blood: Hgb. (Tallquist) varied from 80 per cent on entry to 65 per cent two days before exodus. White blood cells varied from 6000 on first count to 9200 on the evening before death, with a tendency toward a gradual slow rise. Red blood cells remained, within limit of error, at 4,300,000 during the entire course. Smear done on entry showed a normal differential count, and no abnormalities in shape, size or color of red blood cells.

(*g*) Urine showed no fixation of specific gravity and was negative for albumin, sugar and important sedimentary findings, except after cystoscopy, when a large trace of albumin appeared and the sediment showed a large number of red blood cells.

The antemortem diagnosis, therefore, on the basis of the above was metastatic malignancy of the liver and lungs; primary source undiscovered.

Pathology. Autopsy performed thirteen hours post mortem by Dr. Victor C. Jacobson shows the following findings:

General external examination is essentially negative except for a rather pendulous abdomen, marked by many lineæ atrophicæ.

Peritoneal cavity shows no free fluid. The omentum is firmly adherent to the peritoneum along the line of the abdominal scar. The liver is very prominent, being pushed downward and forward, its lower border 15.5 cm. below the xiphoid and 7 cm. below the right costal margin. The spleen is covered by the left lower ribs. The appendix, uterus, tubes, and ovaries are not present, only a short cervical stump remaining. The diaphragm is on a level with the lower border of the third rib on the right and with the fourth rib on the left. The mesenteric lymph nodes are very small and lie embedded in much mesenteric fat.

Pleural cavities are practically obliterated by the adhesion of the lungs to the parietal pleuræ, which is rough and nodular from the presence of innumerable, irregularly rounded projections of tumor, varying in size from that of a pinhead to that of the largest on the diaphragmatic pleura, which is about 2 x 3 x 3 cm. These nodules are dark red, streaked with white, very firm and usually surrounded by radiating, dilated veins. In the right cavity 250 cc and in the left 150 cc of a blood-tinged fluid is found.

Mediastinum. The under surface of the sternum is studded with tumor nodules 0.2 to 2 cm. in size. The mediastinal fat is of normal amount and shows no tumor growths. The organs are in normal position.

Pericardial cavity is normal.

Heart shows nothing of importance.

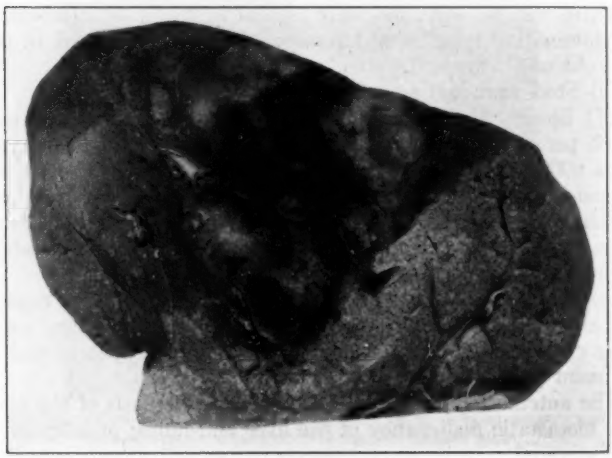

FIG. 3.—Photograph of the liver tumor (much reduced) showing extension into a hepatic vein.

Lungs. The right and left lungs weigh 710 and 705 grams respectively, are similar in appearance and of about half their normal size. The pleural surfaces are rough and nodular, due to the presence of a large number of rather hard, pale white, circumscribed growths, varying in size from 1 mm. to 2 cm. and projecting about 3 mm. above the surface. These are found all over the pleura, and while the lymphatics are fairly prominent, these tumors do not seem to be intimately connected with them. About many are radiating, dilated venules. Between these nodules the tissue is rather elastic, slightly crepitant and grayish red. The glands at the hila and also at the bifurcation of the trachea are 1 to 2 cm. in size, many are very firm, and on section are opaque white,

streaked with red. A lateral incision in each lung (Fig. 4) shows a widespread distribution of the tumor nodules, similar to those on the pleural surfaces. They vary in size as in the pleura and are diffusely distributed throughout the lung lobules. Many are colored with carbon pigment or surrounded by a narrow black ring of anthracosis. The tumor growths appear to arise chiefly in the small arterioles and the picture is much different from that of metastasis by way of the lymph stream. The tissue between the tumors varies in color from gray to deep red and in consistence from elastic to firm and meaty. Thrombi occlude many of the

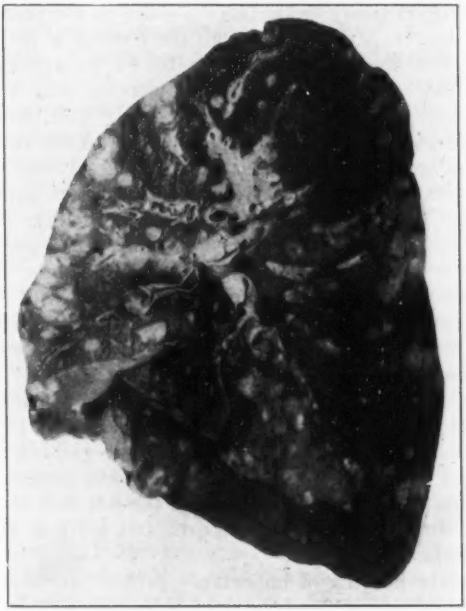

FIG. 4.—Photograph of section through right lung, showing metastatic nodules.

arterioles, but the larger vessels are empty. In some of the bronchioles, dark red blood clots are found in which are small particles of opaque-white tissue, suggesting tumor. The trachea shows moderate injection of the mucosa.

Spleen is about twice its normal size, dark red and firm.

Gastro-intestinal tract is normal.

Pancreas is dark red and rather soft in consistence. The pancreatic duct is dilated, but there is no bile-staining, stone or plug of any kind. The lobules are well marked but hemorrhage has occurred between practically all, with some staining of the lobules.

No fat necroses are seen and the pancreatico-duodenal artery is normal as far as can be dissected.

Liver is much enlarged (weight 2360 grams), particularly in its right lobe, which on its lateral and posterior surfaces is firmly adherent to the diaphragm. This is due to the presence of a mass occupying about half of the right lobe and extending outward so that a protuberance with pearly white borders and a dark red, depressed central portion projects about 1 cm. above the surface over an area about 12 cm. in diameter, forming a growth shaped more or less like a group of rosettes. The diaphragm appears to be invaded and streaks of grayish-white, very probably tumor tissue, run from the liver tumor to the large nodules on the pleural surface of the diaphragm. Sections through the liver (Fig. 3) at various angles show that the gross tumor is limited to the large mass in the right lobe, the remainder of the organ having only a moderate "nutmeg" appearance. This tumor is fairly well circumscribed and its greatest diameter is 15 cm. It is of almost cartilaginous hardness and has no definite capsule, though clearly rounded edges. There is a distortion of the liver lobules adjoining it, probably due to pressure. The tumor is not bile-stained and there is no gross evidence of bile stasis. Dissection shows that the larger bile ducts leading to the tumor abruptly stop when the tumor is reached. Small branches of the hepatic vein in the vicinity of the tumor contain thrombi and a few of them flecks of grayish-white, quite firm tissue, possibly tumor. The ducts and vessels of the rest of the liver show no lesion.

Gall-bladder is but 0.5 cm. from the tumor, but its mucosa moves freely over the subjacent tissues and appears normal. Eight black, faceted calculi, 1.5 cm. in size, lie free in the gall-bladder. The cystic, hepatic and common ducts in the porta hepatis show no stones or tumor. Two lymph glands at the junction of the cystic and hepatic ducts are enlarged and firm, but are pale and do not appear to contain tumor.

Kidneys show nothing of importance except two small cysts in the substance of the cortex of the right kidney.

Genitalia. Only the stump of the cervix remains and a red, pedunculated polyp, 2 x 0.5 cm., is attached to the midportion of the cervical mucosa, bathed in a reddish, mucoid secretion.

Aorta shows moderate intimal thickening of the arch; the vena cava inferior contains no thrombi.

Microscopic Examination. *Heart.* A fairly large area of a section through the left ventricle shows degeneration of the muscle fibers and replacement by young fibroblasts and congested capillaries.

Lung. There are two sections showing processes that are alike. These are for the most part filled with tumor that appears as nests of epithelial cells surrounded by a connective stroma and as cavities lined by epithelial cells of several layers of thickness. Most of

these cavities show a tendency in their walls to grow in toward the center, giving the appearance of an adenocarcinoma. Tumor cells are seen to plug many of the veins. Mitotic figures are numerous. The remaining portions of the sections show congestion of the alveolar capillaries and many small areas of organizing pneumonia. Large numbers of desquamated epithelial cells and a few polymorphonuclear leukocytes are seen in many alveoli. A few of these contain plugs of fibrin and invading fibroblasts. A section of the trachea and attached lymph node shows no tumor.

Lymph node (bronchial) is surrounded by a thick capsule and contains abundant carbon pigment. The central portion shows an extensive invasion of tumor, the cells and their arrangement being similar to the tumor elsewhere.

Diaphragm. The section consists of striated muscle and tumor. The muscle fibers in the region of the tumor are replaced by hyalinized fibrous tissue. Sections of dense fibrous tissue that have become hyalinized in places contain many irregular cavities filled with tumor cells.

Spleen. That of chronic passive congestion.

Liver. There are four sections showing processes more or less alike. The more conspicuous of these are the numerous foci of tumor cells. These appear as elongated and cuboidal epithelial cells, basic stained, having large, finely granular nuclei and a narrow rim of clear cytoplasm. While some of the cells are loosely scattered the tendency is for them to form columns, supported by delicate fibrous strands. In places there are wide trabeculæ of connective tissue. In the portal areas there is a proliferation of fibrous tissue and bile ducts. Many of the latter have an epithelial lining several layers thick, partially occluding the lumen, while in others the epithelial cells have ruptured the basement membrane and invaded the surrounding connective tissue stroma. The tumor cells in general are in every respect similar to those of the bile capillaries, a feature which indicates the origin of the tumor. There is pressure atrophy of many of the liver cells as a result of the tumor invasion and marked congestion of the sinuses. Many show necrosis, particularly about the central areas, where many polymorphonuclear leukocytes are seen in the sinuses. Other liver cells show tremendous fatty infiltration. Some of the smaller branches of the hepatic veins contain tumor.

Kidney. There is but one section, that showing the picture of a chronic passive congestion with thickening of the capsule. There is connective tissue increase and slight thickening of the glomerular capsule with atrophy of the tufts beneath it. In this region two or three groups of tumor cells are seen, both as irregular tubules and as small nests in the connective tissue. A small hemorrhagic infarct is present in the cortex of the kidney.

Pancreas shows acute hemorrhagic necrosis, probably agonal.

Anatomical Diagnosis. Massive adenocarcinoma of the liver (primary), with metastases to the lung, pleuræ, mediastinal lymph nodes and kidney. Pleural effusion (bilateral). Acute hemorrhagic pancreatic necrosis. Chronic fibrous myocarditis. Cholelithiasis. Cervical polyp. Absence of uterus, tubes, ovaries and appendix (operative).

Discussion. The *raison d'être* for the report of this case lies not so much in the underlying pathology which it presents as in the interesting clinical features which make it, I believe, unique among cases of this variety.

Primary carcinoma of the liver is relatively a rare tumor, its average incidence in the autopsy rolls of ten of the world's largest clinics being about one in every thousand autopsies. Eggel[1] reviewed 163 cases reported up to 1901 and some 150 have been added since by various writers, especially Fischer,[2] Acland and Dudgeon,[3] Pepere,[4] Dibbelt,[5] Oertel,[6] Colwell,[7] Polak-Daniels,[8] Wegelin,[9] Grawitz,[10] Gravina,[11] Herxheimer,[12] Hawes,[13] Cade,[14] Loehlein,[15] Wheeler,[16] Karsner,[17] Goldzieher and v. Bokay,[18] Amlinger,[19] Winternitz,[20] Okazski,[21] Muir[22] and Milne.[23]

Generally speaking, from the standpoint of morbid anatomy, primary carcinoma of the liver arises from a proliferation of the liver cells or from the cuboidal or columnar epithelium of the intrahepatic bile ducts. They are divided broadly into three groups: (*a*) Nodular, resembling multiple secondary nodules, except that no primary focus can be found, and constituting, in Eggel's careful review, 64.6 per cent of his cases; (*b*) massive, consisting of a large white or yellowish "mother-tumor," occurring

[1] Beitr. z. path. Anat. u. Physiol., Jena, 1901, **30,** 506.
[2] Virchow's Arch. f. path. Anat., 1903, **174,** 545–563.
[3] Lancet, 1902, **2,** 1310.
[4] I Tumori malign Primarii del Fegato, 1902, p. 171.
[5] Ueber hyperplas., adenom. u. prim. Krebs der Leber, Greifswald, 1903, F. W. Kunike, p. 61.
[6] Virchow's Arch. f. path. Anat., 1905, **158,** 499–515.
[7] Arch. Middlesex Hosp., London, 1905, **5,** 123–141.
[8] Ztschr. f. Krebs forsch., Berlin, 1905, vol. **28.**
[9] Virchow's Arch. f. path. Anat., 1905, **179,** 95–153.
[10] Deutsche. med. Wchnschr., 1905, **31,** 284.
[11] Gazz. internaz. d. Med., 1905, **8,** 63–65.
[12] Centralbl. f. allg. Path. u. path. Anat., Jena, 1906, **17,** 724.
[13] St. Bartholomew's Hosp. Rep., 1905, London, 1906, **41,** 161.
[14] Lyon méd., 1908, **110,** 785–789.
[15] Beiträg. z. path. Anat., etc., Jena, 1907, **42,** 531–558.
[16] Guy's Hosp. Rep., London, 1909, **68,** 225–244.
[17] Arch. d. Med., 1911, **8,** 238–261.
[18] Virchows Arch. f. path. Anat., 1911, **203,** 75–131.
[19] Primary Carcinoma of Liver with Metastasis to the Lungs, Bonn, 1911, J. Trapp.
[20] Johns Hopkins Hosp. Rep., 1916, **17,** 143.
[21] Sei-I-Kwai Med. Jour., Tokyo, 1915, No. 1, vol. **34.**
[22] Jour. Path. and Bacteriol., 1908, p. 287; 1911, p. 389.
[23] Ibid., 1909, p. 348.

usually in the right lobe and forming 23 per cent of Eggel's cases; and (*c*) diffuse, wherein the growth extends widely throughout the organ, perhaps without gross increase in its size, histogenetically practically always spheroidal-cell in type, and numerically composing 12 per cent of the cases. Sauborin,[24] Hanot and Gilbert[25] and others have attempted to add a fourth group, "cancer avec cirrhose," but since cirrhosis is so frequent an occurrence in all groups (various observers reporting it in one-quarter to one-half of all cases), this close interrelation to the original three seems to make this addition superfluous.

Eggel classes but 27 of the 117 cases which are described microscopically as of the massive type, and of these but 3 (or less than 3 per cent) are considered to be of bile-duct origin. Other observers, among whom are Herxheimer,[12] and B. Fischer,[2] have contended that 50 per cent of the cases classed by this author as of liver-cell origin are in reality bile-duct cancers; but their arguments are unconvincing, hence for the present at least we will abide by the opinion of the original observer.

Unfortunately, however, a grouping of the hepatic carcinomata on this basis is not as simple as these headings might lead us to believe, for there is a pronounced overlapping throughout, and in addition there are further subheads separating "solid" and "adenomatous" tumors as well as those of liver-cell and bile-duct origin. Hence we shall not concern ourselves further with the vagaries of classification but rather proceed to a discussion of the case at hand.

Etiologically we are on no more familiar ground than in malignancy elsewhere, though the relative frequency of an alcoholic history, as well as the common coincident hepatic cirrhosis, favors the view that, in a certain proportion at least, "we have a vicarious hypertrophy, which, from some unknown cause, proceeds past its goal and by atypical growth leads to the formation of a tumor" (Orth,[26] Schmeiden;[27]) or, in the words of Rolleston,[28] "There is an acquired habit of proliferation of the liver cells which, starting as a compensatory hyperplasia and thus giving rise to multiple adenomata in cirrhosis, eventually becomes so excessive as to constitute carcinoma." It is interesting that whereas gall-stones are so common a finding in carcinoma of the extrahepatic bile ducts and gall-bladder (in 80 to 90 per cent of cases according to most statistics), in the type under discussion they seem to be but occasional incidental occurrences, found in none of 41 cases and in but 5 of 25 cases in the series reported from two large London hospitals. There are, of course, the usual references to trauma and heredity,

[24] Essai sur l'adenome du foie, Th. doct., Paris, 1881.
[25] Études sur les maladies du foie, Paris, 1888, p. 30.
[26] Path. Anat., 1887, s. 955.
[27] Virchow's Arch., 1900, **154,** s. 290.
[28] Diseases of the Liver, Gall-bladder and Bile Ducts, Macmillan, 1914.

and, under the latter, Hedinger[29] cites an unusual pair of cases in which two sisters, aged seventy-one and seventy-seven years, came to autopsy in his clinic within the same week, each showing a definite primary carcinoma of the liver. However, aside from this single unique observation, the hereditary factor is more conspicuous by its absence than otherwise.

Incidence. (*a*) *Age:* Although Eggel's figures and those of the majority of writers on this subject show that a large majority of cases fall within the so-called "tropic of cancer," Castle[30] has reported 42 cases, all apparently authentic, and to these Griffith[31] has added 15 more, occurring under sixteen years. The relatively high incidence in the first year (28 per cent) points toward a possible congenital factor in many of these juvenile tumors.

(*b*) Sex: Contrary to the finding in secondary carcinoma of the liver, but in keeping with cirrhosis itself, the male incidence definitely predominates (63 per cent in Eggel's series).

Location. Of the above-mentioned 27 cases of carcinoma of the massive type, 18 were in the right lobe alone, 6 in the left alone and 3 showed a generalized infiltration.

Clinical. Symptomatically there is an unusual uniformity in the list of complaints recorded, which consist in the main of general weakness, a sense of epigastric fulness proceeding later to epigastric or right upper quadrant pain, occasional dyspnea and often diarrhea. Physical examination reveals (*a*) jaundice, usually relatively mild, in about 60 per cent of the cases reported; (*b*) ascites, frequently hemorrhagic, in about 58 per cent; (*c*) edema, most often of the lower extremities, in 40 per cent; (*d*) splenic enlargement in 32 per cent; and (*e*) fever, practically always of a very moderate grade, 14 per cent; with (*f*) tenderness on pressure over the hepatic area in a large majority of cases. The postmortem evidence has rather frequently shown pulmonary metastases, contrary to the teachings of most text-books on the subject, but in no previous case which I have found has the new growth there been of sufficient extent or importance to have given abnormal findings on the physical examination of the chest during life.

With the rather sparse signs found over the chest in the present case, our first evidence of the real extent of the pulmonary process came from the observation of the pulmonary "vital capacity" of the patient or the volume in cubic centimeters of "the greatest possible expiration after the deepest possible inspiration," as recorded on the ordinary water spirometer. It is a measurement, in short, of the depth to which the respiration can be increased. Peabody[32] has recently given an admirable discussion of this subject with a thorough review of the literature on it. Normal standards

[29] Centralbl. f. allg. path. Anat., 1915, **27**, 385.
[30] Surg., Gynec. and Obst., 1914, **18**, 477.
[31] Am. Jour. Med. Sc., 1918, **79**, 155.
[32] Oxford Medicine, 1910, **1**, 599–609.

have been established for both sexes with respect to the individual surface area, as determined by the height and weight table of Du Bois.[33] Results in children and in individuals over forty have not been published, but from personal observation in a considerable number of the latter there seems to be a decrease normally to 75 to 80 per cent of the normal standard for younger adults, as the tissue elasticity grows less. However, as the lowering of the vital capacity in the case under discussion was about 41 per cent of normal on entrance, it is seen that the change is pronounced enough to be a distinct guide in diagnosing the scope of the lung pathology, and this was further borne out by the continued fall as the process advanced clinically and roentgenologically.

Summary: 1. The case under discussion is one of primary carcinoma of the right lobe of the liver, originating from the epithelium of the intrahepatic bile ducts.

2. Metastases are demonstrated in the liver substance, in glands at the lung hila, in the kidney and seeded throughout the parenchyma, pleuræ and bloodvessels of both lungs. Numerous thrombi are found in the hepatic veins.

3. Many of the classical features of tumors of this type, *i. e.*, the right upper abdominal quadrant pain, jaundice, ascites and edema, are lacking. The pulmonary symptoms, thoracic pain, dyspnea and hemoptysis, led to the patient's entrance into the hospital and dominated the picture throughout, producing the most interesting phase of the case, the marked reduction in vital capacity as compared with the relative insignificance of the pulmonary signs. The change in vital capacity furnished the first real evidence of the extent of progress of the intrathoracic process, which was later demonstrated in the autopsy room.

In conclusion, the writer wishes to acknowledge his obligation to Dr. Victor C. Jacobson for his kind assistance in the pathological study of the case.

THE EARLY MANIFESTATIONS AND RATIONAL TREATMENT OF TABES DORSALIS.

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Our conception of tabes dorsalis, the most common of the chronic diseases of the spinal cord, has undergone many changes during recent years. That it was in some way related to syphilis was early recognized by Fournier and his contemporaries, but the fact that the common manifestations of syphilis had usually been in abeyance

[33] Arch. d. méd., 1916, **17**, 855.

for many years when the symptoms of tabes made their appearance, led to the belief that it was a sequel rather than a manifestation of an active syphilitic process. It was accordingly considered as a parasyphilitic affair until the modern methods of spinal fluid examination conclusively established its syphilitic nature. It is now believed that infection of the nervous system takes place at the time of maximal spirochetal mobilization in from 25 to 35 per cent of cases, that is during the period of secondary manifestations[1]. It is interesting to speculate why so many years elapse after infection before symptoms appear. Warthin has demonstrated that spirochetes may, for a time at least, lie between the cells of the heart muscle without producing any change in the adjacent cells. It is possible that the same thing obtains in nervous tissue. We know that the changes produced by syphilis are brought about very slowly. Years elapse between the beginning of the perivascular infiltration about the vasa vasora in the adventitia of the aorta and the appearance of aneurysmal symptoms. The same must be true when the nervous system is attacked. In some cases trauma seems to precipitate the symptoms; in others exposure, overwork, excesses, etc., appeared to be responsible. It has been suggested[2] that the initial implantation of spirochetes in nervous tissues does not constitute an infection, as we usually understand it, but produces rather a sensitization or a condition of "hyperallergie." Later, when, as the result of some of the causes already enumerated, there is a fresh mobilization of organisms or their toxins, flooding of the nervous system results, with activation of the previously established foci. Thus it is that a reaction in hypersensitive tissue, even though there be relatively few spirochetes present, may be of serious nature and lead to grave tissue destruction. Before discussing the symptomatology and physical signs it may be well to briefly consider the present conception of the pathology. It is now believed that the degeneration in the columns of Goll and Burdock is not primary but secondary to change in the posterior roots and ganglia. *The process probably begins as a slowly progressive meningitis, often minute in extent, about the posterior roots proximal to the ganglia.* The small vessels of the pia arachnoid show a perivascular plasma and round-cell infiltration. This inflammatory process, possibly by pressure, results in a degeneration of the ganglia and of the centripedal roots, which is followed by an ascending degeneration in the posterior columns. It is at once apparent that *recognition of the symptoms and signs that precede the stage of degeneration is of paramount importance if our therapy is to avail.*

A basilar meningitis is frequently present and implication of the cranial nerves often follows, especially the third, fourth and sixth; in fact, this may be the first evidence of involvement of the nervous system. The most dreaded of all manifestations, optic atrophy, is now thought to be secondary to meningitis. Degeneration of the

peripheral sensory neurons has long been recognized, but the sequence of its occurrence has not been definitely determined. Both Ehrman and Levaditi[3] have shown that the Spirocheta pallida may pass from the primary lesion up the peripheral nerves; they have discovered the organism not only in the lymph spaces of the perineurium, but actually between the nerve fibers.

Orr and Rows[3] have shown experimentally that toxins introduced into the sheaths of the peripheral nerves will produce "tabetic lesions" in the cord; they believe tabes results from lymphogenous infection. From the extensive and varying pathology it is obvious that the symptomatology must be exceedingly diverse and often confusing. Curious complexes arise, due to the fact that certain sensory neurons are in a state of acute irritability causing pain, while others, more or less completely degenerated, cause varying degrees of anesthesia and paresthesia. The difficulty in walking, for instance, so apparently a motor difficulty, is not due to motor-tract involvement but the degeneration of the sensory neurons with resulting loss of the sense of position. Because of the great variety of symptoms we see tabetics seeking relief not alone from their family doctor but from the specialist in "rheumatism," the orthopedist, the gyncologist and the eye, ear, throat and nose specialist. We see them swallowing stomach tubes, duodenal tubes and barium meals; using vibrators and electric batteries; being robbed of their prostates, and periodically having their abdomens explored. One is impressed in taking the history of these unfortunates not only with the long period of time that intervenes between the primary infection and the development of symptoms but by the number of years that often elapse after seeking relief before the nature of the trouble is recognized. In order to illustrate this varied symptomatology I have reviewed the histories of 60 cases comprising hospital, referred and private patients seen during the past few years. Thirty per cent were females and 70 per cent males. The average age of the women was forty years and of the men forty-five years. A history of syphilis was present in 45 per cent of the men but in only 16 per cent of the women. In 4 cases the infection appeared to have been prenatal; in 6 others this was suggested.

Pain is by far the most common symptom complained of. The common term "lightning pains" well describes their sudden onset, stabbing nature and rapid abatement. They were present in over 60 per cent of this series. The pains, however, are not always so intense and characteristic, and sciatica may be closely simulated. Numbness and tingling in the extremities, most commonly in the feet, also "drawing" sensations in the feet, are common symptoms and may precede the pains by a considerable period, but because of their unobtrusive character are often disregarded by the patient. While pain is the chief symptom, careful questioning will frequently reveal that other symptoms, perhaps more characteristic of the

condition than the pain, have existed for some time previously. It is, for this reason, important that a complete history be obtained, whenever patients complain of vague pains in various parts of the body, as the fitting together of isolated and in themselves insignificant data will oftentimes enable one to make a diagnosis that the blood and spinal fluid examinations will substantiate.

CASE I.—When J. H. was thirty-nine years old he began to notice that he would have *sharp, fleeting pains just above his heels in the evening;* if at a meeting he would frequently have to retire, as walking about caused the pains to disappear. There was also a "drawing sensation," as though his feet were in a vise. These pains were suggestive, but their significance was increased many fold by the fact that for several years he had noticed that *he could go for many hours without any inclination to pass his urine,* and that when he did void he passed a large amount. These symptoms slowly increased and his hearing began to fail. About *five years later incontinency* began and the urine became foul. At this time, ten years after the first symptoms and twenty-five years after his chancre had been cauterized, he was referred to a surgeon for prostatectomy. Fortunately the surgeon happened to be the late Dr. O. C. Smith, who recognized a cord lesion and referred him to me for treatment.

Bladder symptoms are mentioned as occurring early in 43 per cent of this series. This percentage I think would have been increased if more care had been taken in investigating it. *Unconscious distention of the bladder is often the earliest symptom,* frequently preceding incontinency by many years. It does not seem that this symptom has received the attention that it merits. The loss of bladder sensibility to distention develops so insidiously that the patient is usually unconscious of it until specific inquiry directs his attention to it. If he has noted it he may likely consider it a convenience rather than an omen of serious import. He may state that he can "go all day" without voiding, and will then pass a large amount. Some delay in initiating the act and in its completion may be present. The diminution of bladder sensibility may precede the development of lightning pains by several years. The characteristic cystoscopic appearance of the bladder wall will be referred to later.

So gradual may be the loss of conductivity of the centripedal neurons that originate in the skin, muscles and joints, and keep us advised as to the position of our extremities, that *unsteadiness in performing accustomed movements may first be noticed by others.* Thus a man who considered himself well was told by friends that he walked as though intoxicated. It is not uncommon for patients to note unsteadiness in going up and down stairs as the first symptom, though they will often acknowledge that their feet had felt numb for

a time previously. The first symptom one woman noticed was that she bumped against the corners of the table when walking about her living room and found it necessary to steady herself; this was several years before the lightning pains began. Another woman first noticed difficulty in threading her needle, apparently due to lack of coördination or diminished tactile sense rather than to poor vision. A married woman, aged forty years, first noticed a numb, dead feeling in the outer aspect of the lower third of the left thigh. Later the same sensation extended over the sides of the chest and the right shoulder. It was not until several years later that the development of severe leg pains caused her to seek relief, at which time the signs of tabes were definite. *Sometimes the symptoms are typical of what we term neurasthenia.*

Case II.—A man, aged thirty-six years, complained of a nervous feeling in his stomach and "gas," and nervousness in his back and insomnia. He was too nervous to work. The stomach symptoms were by far the worst, and a specialist washed his stomach on eighty consecutive days. When I saw him several months later he was an advanced taboparetic.

The marked dissimilarity in symptomatology is well shown by two cases that were in the women's ward on Dr. Cochran's service at the hospital at the same time a year ago. They also illustrate that the physical signs are not always the same.

Case III.—H. H., a woman, aged thirty-nine years, had been in her usual health, save for some blurring of vision occasionally and a slight cough, until four days before admission to the hospital. At this time, while bending over her work, she was seized with a feeling of numbness and a sensation of "pins and needles" around the toes. The legs were very weak and she had difficulty in walking upstairs. The following day the same tingling developed in the fingers of both hands and spread up the arms. The day after admittance to the hospital she could not stand alone. The *pupils were unequal, dilated and immobile, the deep reflexes were absent,* the Wassermann was positive in the blood and spinal fluid and the colloidal-gold test gave a paretic curve.

An entirely different picture was present in the next case.

Case IV.—A married woman, aged twenty-six years, complained of *palpitation and dyspnea.* Eight weeks before she had a curettage following a criminal abortion; one week later she began to have *tachycardia* and became short of breath. A little blood had been present in the urine several times. She was *very nervous,* which seemed to account for the rapid heart action, which was 140, perfectly regular, with all beats coming through to the wrist. A rate of over 120 was maintained for a number of days. She was

emotional and cried a good deal. The urine obtained by catheter always contained red blood cells, which cystoscopy demonstrated came from the kidneys. The amount and gravity of the urine was normal and there was no nitrogen retention, though there was some diminution in the phthalein output. Typical *leg pains were present after antisyphilitic treatment was started;* these focal reactions are very suggestive. *Pupils regular, equal and actively mobile. On admission the knee-jerks were much diminished and unequal; five months later they were absent. Ankle-jerks were present at first, but disappeared several months before the knee-jerks became absent.* Blood Wassermann was positive; spinal fluid Wassermann was positive; colloidal-gold luetic curve.

The pains due to lesions in the upper segments of the cord are less common and more difficult of recognition. They may be very severe and "colicky," or the patient may experience a sense of constriction, as though a rope or a band were drawn about the chest.

CASE V.—M. P., aged thirty-seven years. Eleven years previously and seven years after his initial lesion he began experiencing *severe pains through the lower part of his chest and the upper part of the abdomen,* more marked on the right side. Electricity failing to give relief the right nipple and a small amount of mammary gland immediately surrounding it was removed. The pain persisting, with commendable perseverance, though with questionable judgment, the surgeon removed the other nipple. Eleven years after the pain started he was an advanced tabetic.

CASE VI.—D. J., a woman, aged thirty-six years, complained of *pain under the left scapula.* This was diagnosed as pleurisy, and some relief seemed to follow the application of adhesive straps. It was subsequently present along the right side as well. It finally became more marked and was then described as a sense of constriction, as though something were tied about the chest. Soon the development of gastric crises and the loss of the reflexes placed the diagnosis on a firm basis.

Very distressing are the so-called crises affecting various viscera—stomach, kidney, heart, larynx, etc.

CASE VII.—I have at present a patient, aged thirty-two years, who illustrates the varying nature of the crises. On two occasions, about eight months ago, he was *awakened at night with severe pain "about the heart"— the pains extended into the left arm.* Within a few weeks he had a *pain in the region of the liver,* beginning gradually but soon becoming so severe that morphine was required. This was accompanied by *pain in the right arm.* The next attack affected the precordial region and the left arm. The succeeding one, which was confined to the *hepatic area,* was preceded for a couple of days by

pains in the right arm. In the last attack but one the pain was again in the left side at about the level of the fifth and sixth ribs. The most recent attack was very severe and confined to the region of the right costal border. A positive diagnosis of gall-stones was made by several physicians who saw him, and an operation was urged. In addition to these severe attacks he describes a "soreness inside" across the chest, and has himself observed that the skin opposite the third, fourth and fifth ribs is less sensitive to touch than above and below this area. In two attacks it was observed that the abdominal muscles were held very rigidly, but no tenderness could be elicited; in other attacks the abdomen was soft. The pains which came in waves were very intense. *The pupils were normal.* The deep reflexes were absent; both blood and spinal fluid Wassermanns were positive.

Gastric crises are the most common type and were present in 10 per cent of this series. When they precede the pupillary changes and the loss of the deep reflexes they are very difficult of diagnosis. The moderate leukocytosis that has been present in several of our cases adds to the difficulty. *Severe abdominal pain, accompanied by vomiting but without abdominal rigidity or localized tenderness, should suggest tabes.* The crises are generally described as beginning without prodromata; severe attacks of pain and vomiting lasting for a number of days. In a few cases I have seen the attacks were preceded by two or three days of discomfort and drawing sensations in the lower part of the back, described by one woman as similar to labor pains. While the severity of the pains may suggest gall-stones the most common mistake is to diagnose some stomach lesion. Sufferers from this condition have often been operated upon not once but several times.

CASE VIII.—L. O., aged thirty-six years, who had a chancre years before, was admitted to the Hartford Hospital about ten years ago complaining of *severe abdominal pains and persistent vomiting* of several days duration. Several years before, when he had the same symptoms, he was operated for suspected gall-stones in a hospital in Brooklyn, but none were found. Fifteen months later he was operated in New York for adhesions; six months later, his symptoms persisting, he was again explored in another New York hospital. As he appeared to have an open season for laparotomies the year around it is quite natural that we should emulate the example of the distinguished New York surgeons. Accordingly *the abdomen was opened for the fourth time,* revealing a mass of adhesions.

But this was years ago; today, with the assistance furnished by the roentgen-ray, the blood Wassermann and the spinal-fluid examination such mistakes would not occur. Of course, the tabetic is liable to any other malady to which man is heir, as a recent

patient demonstrated. He had severe upper abdominal pain and the typical signs of tabes, but a negative blood and spinal fluid. Antisyphilitic treatment did not relieve him, so the abdomen was opened and a carcinoma of the gall-bladder was found.

Laryngeal crises are fortunately very rare and occurred in but one of this series.

CASE IX.—M. E., aged thirty-nine years, had very severe *attacks of choking*, first coming on after drinking to excess. He would awaken at night choking and would become deeply cyanosed. All accessory muscles of respiration were called into play. The pulse was of good quality in one attack and very faint in another one. The attack would last from a few minutes to an hour. During the severest attack in 1913 artificial respiration was resorted to, and it seemed as if death would take place at any minute. He had been suffering very severely prior to the time from leg pains and had been given a number of hypodermics of morphine. It is possible that this was a factor, as *tabetics are occasionally met with who stand morphine very badly*. Several years ago I almost lost one patient following the administration of a small amount of codein and morphine for leg pains.

One patient seen several years ago was subject to very severe attacks of pain that were localized in the symphysis pubes. A recent case complains of a pain that "comes quickly" in the region of the sacrum; it extends forward across the lower abdomen, and the patient then experiences the desire to go to stool. An enema, even though no bowel movement results, gives relief for several hours.

Severe pain referred to the kidney, designated as a renal crisis, occurred in 3 patients. In one man, who also had gastric crises, the pain radiated to the testicle. There may be no radiation, the pain suddenly comes on with great intensity, persists for a few minutes and then subsides momentarily, only to recur with stabbing intensity. In 1 very typical case I could elicit no tenderness.

CASE X.—One of the most interesting cases of this series was a man, aged twenty-two years, referred to me by Drs. Kingsbury and Hutchison, to whom I am indebted for the early notes in the case. He complained of *severe pain in the right flank radiating to the penis;* also hematuria and increased frequency, with difficulty in starting the stream. He had had two similar attacks during the two years preceding, and during one of which there had been considerable albumin in the urine. *The pupils and the knee-jerks were normal* and the roentgen-ray for kidney-stone was negative. Cystoscopy by Dr. T. N. Hepburn, who made the following *resume* of his findings:

"It is evident that this man's kidneys are functioning equally

and apparently normally, as shown by their excretion both by indigo carmin and phthalein. His marked *bladder trabeculation* suggests some spinal-cord pathology. The history of urine spasm during his attacks of renal colic with swelling of the extremities suggests that these times he has acute nephritis with hemorrhage. In view of the fact that the ureters admit No. 7 catheters without difficulty under anesthesia and the roentgen-ray being negative, there seems to be no calculous pathology. With his marked bilateral hemorrhages and his normal renal function the diagnosis of essential hematuria seems very possible. His bladder, nervousness with intermittent bladder spasm, suggests the true bladder tic. My personal diagnosis is that he has essential intermittent hematuria with blood-clots forming in his ureters, causing ureteral spasm and secondary bladder spasm which causes his incontinence. My treatment should depend largely upon the spinal-fluid examination and Wassermann."

Both the blood Wassermann and spinal-fluid Wassermann were positive and the patient showed the paretic colloidal-gold reaction. *Two years later the pupils were immobile and the knee-jerks had disappeared.*

This was 1 of the 4 cases in which the infection appeared to have been prenatal.

Drs. Hepburn and Spillane have cystoscoped all of our recent cases and the bladder trabeculation has been found almost without exception. The trabeculation may be due to hypertrophy of the muscles of the bladder resulting from an attempt to overcome the distention that takes place because the sensory nerves of the bladder that initiate the act of micturition are degenerated. We, however, do not feel that tabes is the only cord lesion that will produce trabeculation.

One never ceases to marvel at the extensive pathology that may be present without causing symptoms. I vividly recall a man, brought to the hospital some years ago, because of a minor injury, who had an aneurysm as large as a child's head. He had stoutly maintained that he had no symptoms and refused to remain longer than was required for his scalp wound. Many have seen patients with extensive pulmonary tuberculosis who had at no time any symptoms of this disease. The following case illustrates the necessity for a complete examination irrespective of the patient's complaint and demonstrates that extensive changes of a permanent nature may be present in the nervous system notwithstanding the complete freedom of symptoms.

CASE XI.—C. E., *a robust man*, aged forty-four years, who looked the picture of health, *came to me for an examination of his lungs.* Several years previously he had tuberculosis with bacilli in the sputum. He had been free from symptoms for some time, though

he was recently advised by an eminent specialist in tuberculosis that it was too soon for him to resume his work. He desired the examination in order that he might secure a pension as a Spanish War veteran. He had a very few fine rales on coughing at the apices; they did not, however, suggest activity. His blood-pressure was considerably elevated and there was a heavy trace of albumin in the urine. There was left external strabismus. The pupil of the left eye was normal; that of the right eye was immobile. Both knee- and ankle-jerks were absent. Blood and spinal-fluid Wassermann was four plus and a luetic colloidal-gold curve.

Contrast with this asymptomatic case with definite physical signs, the following case recently seen in whom the symptoms are marked, but the classical physical signs lacking.

CASE XII.—A man, aged sixty-one years, who had an initial lesion twenty odd years ago, complains of severe pains in the legs below the knees, extending down to the ankles. Walking up or down grade makes the pain almost unbearable. He also has sudden sharp pains in the thighs. At night he has a drawing sensation in the feet so marked as to necessitate his getting up to stretch them. This he does by pressing them against the floor or the foot-board of the bed. He usually goes all day with no desire to void. Notwithstanding that *both knee- and ankle-jerks are present and the pupils react to light* his symptoms must be attributed to changes in the posterior nerve roots.

There is still another type of a case entirely symptom-free, and in addition with an entirely negative physical examination, except for a persistently positive blood Wassermann. This is the pre- or potentially tabetic case, which if promptly recognized and adequately treated can often be cured. The following is an example:

CASE XIII.—R. J. was referred for arsphenamine treatment because of *gangrene of the hand*. This improved promptly under injections of arsphenamine, but *the Wassermann test* on the blood *after fifteen treatments*, with a course of iodide and mercury, was *still positive*. A patient whose Wassermann cannot be influenced by a course of eight to ten injections of arsphenamine should always have the *spinal fluid* examined, as it will be found positive in many instances. In this case it was reported *positive in* 0.5 *cc*. The physical examination may be entirely negative or the degree of reaction of the pupils to the light test may be slightly diminished and the deep reflexes perhaps slightly increased.

Occasionally the blood Wassermann may become negative after intravenous treatments, but a positive reaction will be found in the spinal fluid even though there be no symptoms or physical signs pointing to involvement of the nervous system. Accordingly a spinal-fluid examination should be made in all cases at the conclusion of the second course of injections.

Important Points in the Physicial Examination. The Argyll-Robertson pupils, reacting to accommodation but not to light, and the completely immobile pupils, often unequal and irregular in outline, are the usual findings. It should be more generally known that occasionally *one or both pupils may be normal*, especially early in the disease. In 25 per cent of our cases the pupils were normal, though 4 patients, who were followed for several years, subsequently showed the changes characteristic of the disease. In 2 instances one pupil was normal. It is probable that a sluggish and diminished response to light regularly precedes immobility. Quite commonly one sees pupils in which the reaction to light starts promptly but ceases just as it gets under way. In some instances this appears to be due to the adhesions of a previous iritis. Two cases presented a paradoxical reflex when first seen. In 1, six years later, the pupils had become small, irregular and immobile. The other had typical Argyll-Robertson pupils at the end of two years. Save in one instance following hemiplegia, I have never seen the light reflex return. In this case the return was only partial and did not persist.

The knee-jerks were both absent in 60 per cent of our cases, diminished or unequal in 19 per cent and *in* 6 *cases* (10 per cent) *much increased*. It is quite likely that the cases showing greatly increased knee-jerks have some involvement of the lateral column as well as the posterior. Both columns were probably involved in Case I, as his knee-jerks were very active when first seen. The nature of the early pathology is such as to suggest that increase of the reflexes may occur more frequently than has generally been assumed. Two patients who exhibited increased knee-jerks several years ago, and who have had a good deal of treatment, now show normal reflexes. Another patient who had increased knee-jerks several years ago has none at present. *The ankle-jerk* is not recorded in all of the cases, but it *was absent in* 3 *in whom the knee-jerk was present*. In 2 instances the knee-jerk could not be obtained though the ankle-jerk was present. In 1 definite case of tabes and in 1 probable case both knee- and ankle-jerks returned following treatment. A careful examination will often reveal areas of anesthesia, most commonly about the feet. Two patients with girdle pains had an anesthetic band, two inches wide, across the chest. The blood Wassermann was positive in 65 per cent of 54 cases tested. In 38 cases the spinal fluid was examined and the Wassermann was positive in 66 per cent. In a few instances the spinal fluid was positive when the blood was negative. In one adult with a prenatal infection both blood and spinal fluid Wassermann were negative. Another case had repeated examinations made of blood and fluid and only once was a weak positive obtained in the spinal fluid. As the colloidal-gold test was only made in the cases seen recently, they are too few to analyze. We have several times obtained a paretic curve in patients exhibiting none of the symptoms of paresis.

Differential Diagnosis. *Severe pains suggestive of tabes may be due to spondylitis or to faulty posture.* This should be suspected in all atypical cases, especially when the blood and spinal-fluid examinations are negative. Moreover, the tabetics digestive symptoms may be due to ulcer rather than to gastric crises. Occasionally *foci of infection,* especially peridental abscesses, may be wholly or in part responsible for severe leg pains. One patient who had been quite free from lightning pains for some time suffered a great deal from their recurrence following the removal of a number of badly abscessed teeth. Several years ago I mistook a case of alcoholic neuritis in a syphilitic for tabes.[1]

It is stated that fixed pupils may be due to cerebral arterial sclerosis, not the result of syphilis. Such cases are uncommon and difficult of diagnosis, as a negative Wassermann test, of course, does not exclude syphilis. *It is apparent that the diagnosis of tabes does not rest on any one set of data; only by a consideration of the symptoms, the physical signs and the blood and spinal-fluid examinations can we arrive at our diagnosis.*

Treatment. (*a*) GENERAL. Before proceeding with the discussion of spirocheticidal remedies and the methods of administration it is perhaps advisable to refer to a number of important points in the management of these patients that are sometimes overlooked. In the first place *the posture of the tabetic is usually faulty.* He is prone to assume the attitude so characteristic of all asthenic states, namely, abdominal protrusion with thoracic recession, the so-called "debutante slump" resulting in increase of the lumbosacral curve and a tilting forward and downward of the pelvis. The abduction of the feet that occurs with increasing unsteadiness is usually associated with marked pronation and loss of the longitudinal arch. The usual corrective exercises and appliances for these conditions should be prescribed. Patients exhibiting marked ataxia should be given *reëducational exercises. Hydrotherapy* requires no elaborate apparatus, and is especially helpful in some cases. Careful search for foci of infection should be made, as they are sometimes a factor in causing pains. The teeth and gums should receive the necessary attention *before specific treatment is instituted.*

(*b*) SPECIFIC. It is perhaps unnecessary to state that the immobile pupil and absent knee-jerk do not in themselves call for antisyphilitic treatment.

I first saw Mr. B. H. in 1909, when he was aged seventy-four years. He presented the usual signs of advanced tabes, yet with no symptoms. The absent reflexes had been discovered years before. The blood and spinal fluid were both negative a few

[1] The question of "pseudo-tabes" was raised in Case III, who was somewhat alcoholic. A neuro-syphilitic might of course have alcoholic neuritis but the pains and tenderness commonly met with in neuritis were absent, while the bladder trabeculation so common in tabes dorsalis was present.

years later. I have seen him occasionally since then, the last time a few months ago, when he was "holding his own" pretty well, notwithstanding his eighty-five years. Insofar as I know he has never had any active antisyphilitic treatment.

It is impossible to formulate a plan of treatment suitable to all cases. Individualization, always important, is particularly so with this group. It is rather generally believed that fewer of the nervous reactions occur if mercury and iodide are given for a short time, three or four weeks, before arsphenamine is started. The frequency of treatment depends on the results to be expected. If we believe we can annihilate our enemy by assault, as is possible when dealing with a primary lesion, a few intravenous injections may well be given at two- or three-day intervals. When, however, the enemy through long years of preparation is well entrenched the assault is ill-advised; much more can be gained by a prolonged siege. Accordingly, in tabetics we will do well to give injections at weekly intervals for the first two months, during which time iodides and mercury either by inunctions or injections may safely be administered if one be on the alert for evidences of renal intolerance. Another month of mercury, then a rest period of a month or two, and then another course of arsphenamine injections, are safe procedures to follow. *When the symptomatic response to intravenous treatment is unsatisfactory, or when we are not successful in reducing the Wassermann or colloidal-gold reaction of the spinal fluid, intraspinal treatment should be used.*

The indications for intraspinal treatment in tabes may be found outside the nervous system as when a serious cardiovascular lesion makes the repeated intravenous injection of arsphenamine a hazardous procedure. I believe it is also desirable to institute both intravenous and intraspinous treatments as soon as possible in patients exhibiting a paretic colloidal gold curve unaccompanied by paretic symptoms. The so-called "paretic curve" is probably indicative of serious parenchymal involvement but not necessarily paresis. A limited experience in the treatment of paretics has been rather discouraging.

The original Swift-Ellis method is generally conceded to give the best results. The reactions are less than with any of the modifications or substitutes that have been suggested. After a thorough trial of the fortification method suggested by Ogelvy, Fordyce has gone back to the original and simpler technic. It is not my brief to argue the *rationale* of intraspinal treatment; this has been done by far abler men. The fallacy of the claim that the good results are due to the drainage incident to the treatments has recently been shown by Fordyce,[4] Stokes,[5] and Osborne and Keidel and Moore,[6] all of whom obtained prompt clinical and serologic improvement when intraspinal treatments were substituted for drainage. Solomon, who for years advocated only intensive intravenous treatment, now employs intraspinal therapy in suitable

cases. The recent work of Dandy,[7] with cerebral pneumography, has shown that when there are no adhesions at the base of the brain all the deep and superficial spaces may be reached by the intraspinal route. It may be found advisable in certain cases to have a cerebral pneumograph made before employing intraspinal treatment to determine the patency of the spaces. It is a mooted point whether the injection of an irritating substance subdurally increases the permeability of the choroidal plexus. As there is some evidence to suggest that this may occur we have recently been giving our intravenous injections within an hour after the intraspinal, the serum for the latter having been obtained the day previously from another patient. As yet we have no opinion as to whether this reversal of treatments is of any special value. The method, however, is quite as well borne as the original technic.

How many treatments shall we give the tabetic? Two or three courses may be if he is fortunate in having the diagnosis made at the first inception of symptoms, or better still by spinal-fluid examination when asymptomatic and in the pretabetic state. When not recognized until the pathology is extensive, after the first two or three courses, he will probably require occasional treatments all his life. *Even though there be advanced nerve degeneration it often happens that there are some neurons still intact and capable of carrying on with assistance.* Active treatment in these cases will sometimes restore the latter to functional efficiency. This is occasionally demonstrated by the improvement in the vision of patients who from the ophthalmoscopic standpoint have optic nerve atrophy. The degree of improvement that sometimes obtains even when the treatment is deferred until many years after the onset of symptoms is very gratifying. The first case mentioned in whom treatment was not instituted until twenty-five years after the chancre and ten years after the beginning of symptoms has greatly improved in his general health. He no longer has pains, though he occasionally has numbness in his feet at night. During the past eight years he has received thirty intravenous and twenty-six intraspinous treatments. He has worked steadily since the treatments were started and has never been absent from his work through illness, except for a few days at the time of treatment, a record that is not equalled by anyone in the office where he is employed. He is still incontinent at night, but less so. He walks much better and each summer works daily in his garden. The knee-jerks, which were greatly increased when treatment was started, are now normal. The blood Wassermann is negative; the spinal fluid still shows a positive Wassermann in 0.5 cc and a weak leutic curve.

Even more striking were the results obtained in Case III, the woman who could not stand alone. Reëducational exercises were started at the same time that antisyphilitic treatment was instituted. As she had a paretic colloidal-gold reaction, though without any

symptoms of paresis, she was placed upon combined intravenous and intraspinal treatment, with mercury inunctions and potassium iodide. In less than two weeks she was beginning to walk, and in one month the knee and ankle reflexes had returned, though the pupillary reflex did not return. As she had a chronic tuberculous process at the apices with bacilli in the sputum, she was sent to the state sanatorium, returning to the hospital every two or three weeks for treatment.

She was given fifteen intravenous and seven intraspinal treatments in addition to several months of mercury inunctions. The spinal fluid Wassermann at first was positive in 1 cc. This soon became positive with smaller amounts (0.4 and 0.2). It is now, one year later, negative with 2 cc (both plain and cholesterinized antigens). The first colloidal gold was 555443100. The most recent report was 554330000. The blood Wassermann, at first strongly positive, is at present plus minus. The only symptom metioned at present is an occasional drawing sensation in one of the toes.

After observing the marked improvement in her general condition and gain in weight since going to the sanatorium, one wonders if tabetics might not hasten their recovery by "taking the cure" while undergoing specific treatment. Though she is symptom-free, she still has a positive Wassermann in the spinal fluid and the paretic curve persists after fifteen intravenous and seven intraspinal treatments.

We should never lose sight of the fact that we are treating a patient as well as a disease. The number of treatments depend upon three things: (1) The effect on the symptoms, (2) the effect on the Wassermann reaction and (3) the effect on the patient. *Continue the treatments until the symptoms subside and the Wassermann is negative if the general condition of the patient shows improvement.* When after several courses of arsphenamine injections the general condition is not satisfactory, though the symptoms may be less, always consider the possibility of an intercurrent infection, especially tuberculosis. Discontinue all antisyphilitic medication for several months, get the patient outdoors and employ all possible aids to build him up. With an improvement in his general resistance the Wassermann may become negative.

Summary. 1. It is generally believed that infection of the nervous system takes place very early during the secondary stage, at the time of maximum spirochetal mobilization.

2. While it has been estimated that 25 per cent of poorly treated syphilitics subsequently develop syphilis of the nervous system, less than 3 per cent of cases treated intensively during their primary stage show changes in the spinal fluid at the end of treatment.

3. A spinal-fluid examination should be advised at the conclusion of the second series of arsphenamine treatments. It is imperative in all "Wassermann-fast" cases.

4. A complete history is of the utmost importance in detecting early cases. It will sometimes be "positive" when the serology is negative. Next to darting pains, bladder symptoms, especially unconscious distention, appear to be of special significance.

5. The pupils may be normal, the deep reflexes present, yet the symptoms may be due to early meningeal changes about the posterior nerve roots.

6. Arsphenamine intravenously, with mercury and the iodides, will prove sufficient in many cases, especially the early ones.

7. When the symptomatic or serologic response to intravenous treatment is unsatisfactory, or when a grave cardiovascular lesion coëxists and makes frequent intravenous treatments hazardous, intraspinal treatments should be instituted.

8. Serious results are more liable to follow repeated series of intravenous injections than properly administered intraspinal treatments.

9. The amount of treatment should not be determined solely by the Wassermann test; the general condition of the patient is deserving of more consideration than it often receives.

Conclusion. The rational treatment of tabes should include not alone the administration of antisyphilitic remedies but the employment of all known agencies for the improvement of the general health, together with periodic examinations of the patient, his blood and his spinal fluid throughout his life.

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THE QUESTION OF THE USE OF ANESTHESIA IN LUMBAR PUNCTURE.

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Whether or not anesthesia, either local or general, should be used in lumbar puncture is a subject upon which some little diverg-

ence of opinion exists. Inasmuch as the employment of a general anesthetic is not without an element of danger, and adds to the risks of an operation which without it has a mortality certainly no higher than that attributable to most general anesthetics themselves, it would seem that the necessity for their use would be a point of some importance. In the absence of any detailed treatise on this phase of the operation of rachientesis it may be of some practical value to draw a few conclusions as to the factors that would decide the operator in his employment of anesthesia in the procedure.

General Anesthesia.—Most authorities of extensive experience, among them Ravout,[1] Neal and DuBois,[2] and Sophian,[3] are of the opinion that general anesthesia is not needed. Quincke,[4] in his original and masterly description of the operation, stated that anesthesia was not essential, with the exception of very rare cases of delirium of a violent type. Howell,[5] however, believes a general anesthetic necessary in children owing to the danger of a sudden movement on the part of the child causing breaking of the needle. Landon,[6] although he does not generally employ anesthetics, sees no objection to their use. Concetti[7] does not administer chloroform in most cases, but has had recourse to it in very nervous children who were greatly agitated, especially when there was marked rigidity of the spinal column. Jelliffe and White[8] have made use of anesthetics if marked tenderness or opisthotonos is present.

In an experience of over 1000 lumbar punctures performed in a variety of meningeal conditions in both children and adults the writer has only seldom seen patients in whom a general anesthetic was required. It is very rare that a child is delirious and restless enough as to require anesthesia. In fact, it may safely be said that if someone is at hand who can properly hold the patient it can almost always be dispensed with. The pain accompanying the introduction of the needle is so transient, and the time required to penetrate to the subarachnoid space of a child is so short (a few seconds), that it seems scarcely justifiable to make use of a general anesthetic. Likewise in adult patients if the operator is skilful the operation is also only a matter of but a few moments. With the proper type of needle and with a sharply beveled point the introduction is but momentarily painful. If the physician is unfamiliar with the procedure or the puncture is difficult, due to anantomic configuration, it may be advisable to resort to local, but surely not to general anesthesia.

[1] Translated by O. Mulot: Am. Med., **7**, 563.
[2] Am. Jour. Dis. of Children, **9**, 1.
[3] Epidemic Cerebrospinal Meningitis, St. Louis, 1913, p. 206.
[4] Die Technik der Lumbalpunktion, Berlin, 1902.
[5] Clin. Jour., London, January 15, 1913.
[6] Lancet, April 16, 1910, p. 1057.
[7] Annales de médecine et chirurgie infantile, 1899.
[8] Modern Treatment of Mental and Nervous Diseases, Philadelphia, 1913, p. 280.

General anesthetics are obviously contraindicated in rachientesis in patients who are very ill, giving the procedure an element of risk proportionate to the condition of the patient and to the severity of the disease in which it is employed. In this connection consideration and due weight must be given to the possible after-effects of the anesthetic on the heart and kidneys and the immediate effect on the heart, the respiration and the blood-pressure, all of which may be already affected by the particular disease in which the operation is performed. Then again the recognized danger of general anesthesia in patients with atheromatous arteries, or in those with diabetes or brain tumor, must not be forgotten.

In many cases of meningitis the mental apathy or stupor of the patient renders anesthesia entirely unnecessary. Even in the violently delirious it is evident that anesthetic cannot be used for each daily puncture. In some it may be demanded for the first puncture or two, but then must be dispensed with.

In very nervous adults not acutely ill on whom the operation is to be performed, for diagnostic or therapeutic purposes, a general anesthetic is practically never required. If needed local anesthesia by cocain will usually be sufficient. In rachientesis for spinal anesthesia it is obvious that a general anesthetic is not to be considered.

There are only a few instances in which it may be employed with advantage. It may at times be necessitated by exceedingly delirious and violent adults who are so robust that they cannot be controlled by any other means. Certainly, the struggling which in some instances follows an attempt to hold such patients will place as much strain on the heart and influence the blood-pressure more than the cautious use of an anesthetic. An additional danger is also thereby avoided, the possibility of the needle being broken. Under such circumstances one may have at times to resort to an anesthetic. Likewise in the violently insane anesthesia may be required.

We have never found it necessary to employ anesthesia for either opisthotonos or marked hyperesthesia in meningitis patients. Ashhurst[9] believes it should be used in cases of tetanus. Certainly, lumbar puncture is rendered much easier and the operation is more satisfactorily completed when a light chloroform anesthesia is used.

As to the general anesthetic to be employed when such is demanded, Sophian[10] and Ker[11] believe that chloroform is the best. Certain authors make use of ether. Thus, Nissl[12] employs the latter in lumbar puncture in the insane. Bloodgood and McGlannon[13] recommend that ether or nitrous oxide and oxygen should be used

[9] Am. Jour. Med. Sc., 1913, **146**, 92.
[10] Loc. cit.
[11] Infectious Diseases, London 1909, p. 509.
[12] Jour. Nerv. and Ment. Dis., May, 1907, p. 312.
[13] Musser and Kelly's Handbook of Practical Treatment, Philadelphia, 1911, **1**, 604.

to secure relaxation if opisthotonos is marked, as in cases of tetanus. We believe with Sophian and Ker that chloroform is preferable. The patient can be much more rapidly anesthetized than with ether, the stage of excitement is not so marked, the quantity of the anesthetic required is very much less and the slight degree of anesthesia, which is just sufficient for the operation, is readily obtained. Moreover the after-symptoms are not nearly so troublesome. One must, of course, bear in mind that the contraindications to chloroform, especially in patients with fatty degeneration of the myocardium, appertain here as elsewhere. In order to avoid the possibility of any accidents the anesthetic should be given slowly, well diluted and the patient put under gradually.

It is often possible to avoid the use of a general anesthetic in delirious, excitable or very nervous patients by giving two hours before puncture a hypodermic injection of morphine and atropine sulphate in amounts proportionate to the age. For adults, morphine sulphate gr. $\frac{1}{4}$ and atropin sulphate gr. $\frac{1}{120}$; for children in proportionate doses. Ker makes use of similar injections, supplemented by the administration of 2 oz. spiritus frumenti fifteen minutes before operation. A somewhat smaller dose (℥ss to ℥ij) may certainly be given in many instances, more especially to those accustomed to the use of alcohol.

Many patients with meningitis may be kept quieter throughout the operation by using what Sophian terms "water anesthesia," having the patient sip water through a straw during the procedure.

In puncturing patients in whom resistance is expected, or who are so nervous or delirious that it is anticipated that the proper position for operation cannot be maintained once the introduction of the needle has been started, it is of invaluable assistance to secure them in the following manner: The diagonally opposite ends of a full-sized bed-sheet are taken hold of by two persons and twirled into the form of a rope. With the patient in the proper posture on his side this prepared sheet is placed under his knees and then the two free ends are drawn upward, flexing the lower limbs well up toward the abdomen. The ends are then crossed and used to encircle the arms above the elbows, and from there are brought over the shoulders and knotted securely in the back. Many patients who would otherwise require several assistants to hold them or a general anesthetic may be satisfactorily treated when secured in this way.

Local Anesthesia.—The question of local anesthesia is of much less relative importance than that of general anesthesia. Nevertheless, under certain circumstances the injudicious employment of some local anesthetics, especially in meningitis, may further complicate the subsequent treatment of the case.

While many writers, among them Porter,[14] Stewart[15] and Jelliffe

[14] Southern California Practitioner, September, 1912.
[15] Diagnosis of Nervous Diseases, New York, 1912, p. 403.

and White,[16] advocate the more or less routine employment of local anesthetics either by means of cocain or a spray of ethyl chloride, others restrict their use to particular types of cases. Gray[17] introduces 10 to 20 minims of a 3 per cent solution of eucain under the skin at the site of puncture as a preparation for rachientesis in spinal anesthesia in children. Barker,[18] however, in performing the operation for the same purpose in adults, does not find this preliminary preparation necessary. Howell,[19] Clergier,[20] Neal and Du Bois[21] do not believe any local anesthetic required. Duflos[22] allows a little ether which has been used to wash the region to remain and evaporate. Rosenthal[23] finds the operation particularly facilitated by a progressively deep infiltration with 0.5 per cent solution of cocain two minutes before puncture.

We have rarely found it necessary to utilize any local anesthetic in our patients. In children the subarachnoid space is relatively superficial, varying in depth from 3 to 4.5 cm., depending on the age. For this reason when the back is well arched and the operator experienced the needle penetrates the dura almost immediately after it passes through the skin. The pain is therefore very transient, the skin and dura being the only sensitive tissues traversed. While local anesthesia has the advantage of diminishing somewhat the pain of the skin puncture, it cannot affect that of the deeper tissues. Its disadvantages, which are mentioned below, in most instances offset this slight diminution of pain. It may safely be said that in young patients it is rarely required with the exception of those on whom the procedure is performed preliminary to the administering of a spinal anesthetic. Under such conditions a superficial or progressively deep infiltration with cocain or one of its derivatives may be serviceable in enabling the operator to better keep the confidence of his patient during the subsequent operation.

In adults local anesthetics are demanded only in exceptional instances. When only one puncture is to be performed in a patient not acutely ill the decision rests with the physician. In very nervous individuals it may be required to avoid a general anesthetic. It often impresses the patient as a more humane method of procedure and must be considered accordingly under such circumstances.

In many cases of meningitis the mental state of the patient makes any anesthetic unnecessary. In all instances in which repeated punctures are to be employed, as in the various types of meningitis, poliomyelitis, etc., the repeated use of cocain, either superficially or deeply, is open to the decided objection that it may inflame the tissues and thus open the way to infection, interfering seriously with subsequent treatment.

[16] Loc. cit.
[17] Lancet, September 25, 1909, p. 913.
[18] British Med. Jour., **1**, 665.
[19] Loc. cit.
[20] Thesis of Paris, 1904–1905, Paris, 1905.
[21] Loc. cit.
[22] Thesis of Paris, 1901–1902, No. 7.
[23] Paris médicale, August 12, 1916, p. 142.

Ethyl chloride is particularly objectionable as a local anesthetic in both children and adults if the patient's spine is at all hyperesthetic. Moreover, by hardening the skin over the site of puncture it interferes with the clearly defined sensation of touch which is so important in starting the introduction of the needle in the proper direction. In adults it is practically useless because its transient anesthetic effects are exerted upon the cutaneous tissues, which are the source of only a small part of the pain. Adult patients experience most discomfort from striking the spinous processes, the lamina or the nerve roots of the cauda equina, as well as when the needle passes through the ligaments and the dura. Progressively deep infiltration with cocain is the only method which even noticeably alleviates the pain of the operation. Finally, it may be said that local anesthesia is rarely required by one skilled in the technic of the operation.

Summary. 1. General anesthesia is very rarely required in performing the operation of rachientesis. A child is seldom delirious and restless enough as to require a general anesthetic, and it does not seem justifiable to make use of one in an operation which can be so quickly performed and in which the pain is so transient. Likewise in adult patients, if the operator is skilful only a few seconds are required to penetrate to the subarachnoid space, and the pain is only momentary.

2. General anesthetics are very much contraindicated in persons who are seriously ill, giving the procedure an element of risk proportionate to the condition of the patient and to the severity of the disease in which it is employed. The immediate effects of the anesthetic upon the heart, the respiration and the blood-pressure, and the remote effects upon the heart and kidneys, all of which may be involved by the particular disease in which the operation is performed, must not be forgotten.

3. The contraindications to anesthesia in patients with atheromatous arteries, or in those with diabetes or brain tumor, appertain here as elsewhere.

4. The only classes of patients in whom general anesthesia may be demanded are those who are exceedingly delirious and robust adults who cannot be controlled by any other means. The struggling which ensues on any attempt to hold such individuals will place as much strain on the heart and influence the blood-pressure more than the cautious use of an anesthetic.

5. In puncturing insane patients under similar circumstances general anesthesia may at times be required.

6. Rigidity of the back and opisthotonos, unless it is so extreme as to prevent the introduction of the needle, are not an indication for a general anesthetic.

7. Likewise in very nervous patients general anesthesia is not necessary. A local anesthetic will be sufficient.

8. When demanded the anesthetic which it is preferable to use is chloroform. The patient can be much more rapidly anesthetized than with ether, the stage of excitement is less and the quantity of the anesthetic required is very small. It should be given very slowly, well diluted and the patient put under only lightly.

9. In many delirious and excitable or very nervous persons the use of a general anesthetic may be avoided by injecting hypodermically, two hours before the operation, morphin sulphate gr. $\frac{1}{4}$ and atropin sulphate gr. $\frac{1}{120}$ (for an adult). This may be supplemented, especially in the case of alcoholics, by a dose (℥j to ℥ij) of spiritus frumenti fifteen minutes before puncture.

10. Water anesthesia, allowing the patient to sup water during the operation, is helpful in keeping some patients, especially those with epidemic meningitis, quiet during the treatment.

11. In puncturing patients in whom resistance is expected, and who are so nervous or delirious that it is anticipated the proper position cannot be maintained, it is of invaluable assistance to secure them by means of a sheet twisted into the form of a rope and applied as described above.

12. Local anesthetics are rarely required in children with the exception of those in whom rachientesis is performed preliminary to the administration of a spinal anesthetic.

13. In adults local anesthesia is needed only in exceptional instances. When only one puncture is to be performed the decision rests with the operator. It often impresses the patient as a more humane method of procedure, and must be considered accordingly.

15. In all cases in which several punctures are necessary the repeated use of cocain, either superficially or deeply, is open to the decided objection that it may inflame the tissues and thus open the way for infection. Ethyl chloride is unpleasant if the patient's spine is hyperesthetic. Moreover, by hardening the skin over the site of puncture it interferes with that clearly defined sensation of touch which is so important in starting the introduction of the needle in the proper direction.

A CLINICAL REPORT OF TWO CASES OF AGENESIS (CONGENITAL PARALYSIS) OF THE CRANIAL NERVES.

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From time to time cases are encountered that present functional defects dependent upon arrested development of certain structures. Deficiency in development may affect more than one system of

the body, or it may be confined to structures involving one system alone.

The two cases I wish to report presented the rare condition of complete absence of function of certain cranial nerves; it was noted at birth, persisted, and was caused, I believe, by a lack of development of their nuclei of origin. This type of cranial nerve paralysis was first described by Möbius in 1892,[1] under the title of "Infantile Nuclear Atrophy." This observer collected 44 cases in which there was absence of function of the cranial nerves, the defect appearing in various combinations.

Möbius was able to prove the congenital origin of some of these cases, whereas in others the origin was uncertain; he believed, nevertheless, that all his cases were caused by a lack of development of the cells of origin of the cranial nerves or to defective vital endurance in these structures. Other observers since then have employed the term "aplasia of nerves" to denote the same condition.

Gowers[2] used the term "infantile oculofacial palsy" to describe defect of the facial and ocular nerves. I would suggest the term "agenesis of the cranial nerves" to describe a lack of development of these structures.

Although many different terms have been employed to describe the condition, the essential point is that the defect is a congenital one and is, therefore, present at birth, although in some instances nothing abnormal may be discovered by the parents until some time has elapsed, the true nature of this type of paralysis becoming thus confused with conditions that are acquired after birth and that are due to other causes.

In the cases reported here difficulty in using the lips for sucking first attracted attention, and paralysis of the facial muscles was noted almost immediately after birth.

H. M. Thomas[3] described similar defects occurring in two brothers. Fry and Kassack[4] also refer to the literature on the subject, and report the case of a girl, aged eleven years, in whom there was congenital paralysis of the seventh nerves on each side and an absence of lateral movements of the eyeballs, mandible and tongue, and a teratologic absence of the left breast.

A similar condition affected the brother of my second case. The tendency of congenital cranial nerve paralysis to occur in more than one member of the same family suggests the possibility of hereditary influence. True heredity, however, requires the transmission of the physical nature of the parent to the offspring, so that in this sense these defects cannot be regarded as being strictly

[1] München. med. Wchnschr., January, 1892, p. 17.
[2] Diseases of the Nervous System, **2**, 197.
[3] Jour. Nerv. and Ment. Dis., 1898, **25**, 571.
[4] Arch. Neurol. and Psych., December, 1919, **3**, 638.

hereditary in nature, although the familial tendencies are quite marked.

The exact cause of developmental defects remains obscure and all explanations are inadequate. Nevertheless, the influence of deficient nutrition and disease, or of any other temporary abnormal condition of the parents, on the child before birth cannot be disregarded. Individual variations are well known. The physical difference between parents and offspring is due to the diversity of external influences.

Crouzon, Tretiskoff et Behague[5] have described the postmortem findings as affecting the nervous system in a case of familial external ophthalmoplegia, in which there was atrophy of the ocular nerves in association with an obscure type of fibrous meningitis, with integrity of the nucleus of the third cranial nerves, although these cells had undergone secondary degenerative changes. These authors admit that it is difficult to explain why the meningitis should be familial in character.

Whatever the true explanation may be it is obvious that more than one pathologic condition that may produce the congenital or familial type of congenital nerve paralysis must be present and the different combinations of cranial nerves may be found in different cases.

The clinical diagnosis must necessarily depend upon the discovery of the lack of function early in life, *i. e.*, shortly after birth, and the exclusion of other causes of cranial nerve paralysis.

In the following cases the upper portions of the face on each side were just as severely paralyzed as the lower portions of the face, therefore the lack of function conformed to the peripheral type of facial palsy.

Prognosis is necessarily unfavorable, and it would seem important to realize that such procedures as anastomosis with the hypoglossus for the restoration of function in the seventh nerves are useless.

CASE I.—Patient, aged thirteen years, consulted Dr. Frazier (who has kindly allowed me to refer to the notes) March 7, 1921, because of bilateral facial paralysis.

History. Father and mother were first cousins. Mother's first pregnancy ended in miscarriage. Patient was the second child; the third, fourth and fifth children are normal, but the sixth is affected by exactly the same condition as the patient, the defect having been noted at birth. The patient was born at full term without complications and appeared normal. The mother noticed, however, that the child had considerable difficulty in nursing, due to the fact that she could not control and use the facial muscles,

[5] Rev. neurol., 1921, No. 5, p. 488.

and particularly the lips, in sucking. The condition was disregarded, but when the child was about four months old it was noticed that she was unable to smile, and since then she has presented the appearance of complete bilateral peripheral facial paralysis. On examination by Dr. Frazier and myself nothing abnormal could be found except impairment of hearing on both sides, as tested by holding a watch close to her ear; she was unable to hear the ticking at a distance of five or six inches. Vision was normal and the mental and physical condition showed no abnormalities.

FIG. 1.—Case II. Showing patient's inability to blow out a lighted match because of not being able to pucker the lips due to muscular weakness.

FIG. 2.—Case II. Showing inability to elevate the eyeball when looking upward, and inability to move the facial muscles.

CASE II.—Patient, a girl, aged ten years, was admitted to the University Hospital Dispensary February 14, 1921. Mother died with gall-stones. Father, one brother and three sisters living and well. The father states that his first child died when two months old, the second died of injury when eight years old, and the third

pregnancy terminated in a miscarriage. Patient said to have been born at full term, the labor having been normal. Appeared healthy at birth but did not have a bowel movement for the first four days, a condition that was attributed to paralysis of the intestine, and was relieved by the insertion of a rectal tube, after which there was no further difficulty. Parents believed that the child's vision was normal at birth, and state that nothing abnormal was observed until she was one month old. At this time the eyes appeared to be "crossed," and she had some difficulty with her lips in sucking the bottle. About the same time it was noted that the child was unable to close either eye completely and that the facial muscles were not moved in a normal manner, a condition that was more pronounced on the right than on the left side, and that has steadily persisted. The child was unable to sit up until she was nearly a year old, but since then she had developed normally, and is now robust and healthy.

Examination. Neither eye can be moved outward, but both eyes can be rotated upward and downward, but not symmetrically. The pupils react promptly to light but not to convergence. Both sides of the face are completely paralyzed. Neither eye can be closed. On attempting to show her teeth there is a slight movement of the muscles of the lower angle of the mouth on either side, this being due entirely to the action of the platysma myoides. She cannot blow out a lighted match held close to her face.

Although the parents declare that this condition was not present at birth, and was first observed when the child was one month old, it seems to me highly probable that the paralysis was congenital, their statement to the contrary notwithstanding.

REVIEWS.

THE VITAMINE MANUAL. A PRESENTATION OF ESSENTIAL DATA ABOUT THE NEW FOOD FACTORS. By WALTER H. EDDY, Associate Professor of Physiological Chemistry in Teachers College, Columbia University. Pp. 121. Baltimore: Williams & Wilkins Company, 1921.

THIS treatise gives a comprehensive, concise account of the present knowledge of vitamines. The discovery of vitamines is described. An account is given of the attempts to determine the chemical nature of vitamines and of the technic for the biological tests to determine the presence of specific vitamines, including the proposed yeast test for vitamine B. The chapter on the sources of vitamines gives, in tabular form, a review of the data on this subject as collected by both British and American investigators. The chemical and physiological properties of the three well recognized vitamines (fat-soluble A, water-soluble B, water-soluble C) are discussed separately. The concluding chapters tell "how to utilize the vitamine in diets," and describe the avitaminoses or deficiency diseases which are produced by lack of vitamines in the diet. Eddy here recognizes beriberi and scurvy as deficiency diseases, and adds "rickets or rachitis seems well on the way to acceptance though the specific vitamine absent in this case is not yet positively identified. Pellagra still resists the efforts of the vitamine hypothesis to bend it to that theory and its etiology is still obscure." A bibliography of 28 pages is appended, covering the literature up to April, 1921; the full title of each cited paper is given. The treatise is intended for both the student and the layman. J. S. H.

BOWEL DISEASES IN THE TROPICS. By SIR LEONARD ROGERS, M.D., etc., London School of Tropical Medicine. Pp. 475; 10 plates; 71 tables and maps. London: Henry Frowde, Hodder & Stoughton, 1921.

ELEVEN and nine years ago, respectively, the author first published books on cholera and the dysenteries. These were reprinted during the war, and are now brought together in a single volume, having been revised and brought up to date, in accordance with the writer's further extensive experience. In addition, a chapter on sprue has been incorporated.

From every point of view, these three diseases are presented in a masterly fashion. A very interesting series of maps has been drawn showing the direction and rapidity of spread of the various cholera epidemics of the last century, from their origin in Bengal, either over the land route through Mesopotamia and Russia to western Europe, or else by the sea route to the Red Sea ports and so to the Mediterranean.

The pathology is very adequately treated, the high points being the colored illustrations of dysentery lesions and the discussion of the pathogenesis of sprue. The author inclines to the view that two organisms play a part in the etiology—a streptococcus of the viridans group (Rogers) and a Monilia (Manson-Bahr and Ashford).

But it is when we come to the symptomatology and treatment of cholera and amœbic dysentery that we find the most valuable pages. For Rogers is the greatest authority of all time on these two diseases. He will always be remembered as the man who revolutionized the treatment of cholera by introducing the intravenous injections of hypertonic saline solutions, thereby reducing the mortality of the disease from 60 per cent to 33 per cent, and as the first one to make clinical use of emetin injections in amœbic dysentery (1912). It is fascinating to read the reports of his first cases so treated, since they mark two of the brilliant successes in the history of medicine. M. N.

PRACTICE OF UROLOGY. By CHARLES H. CHETWOOD, F.A.C.S., former Professor of Genito-urinary Surgery, New York Polyclinic. Third edition. Pp. 806; 310 illustrations (7 in color). New York: William. Wood & Company, 1921.

THE third edition of this most worthy text-book has appeared. Standing, as it does, as one of the best rounded expositions of the specialty of urology; better illustrated than any book of its size; thoroughly modern and up to date in every subject, while devoid of many of the older empirical ideas; it may well be recommended to the student—undergraduate and postgraduate alike.

The material is well arranged into brief chapters in their proper sequence and presented in a very readable style with the reasons of the author's opinion, as to the choice between methods of diagnosis or treatment, clearly expressed. Chapter I, on anatomy, contains numerous errors that have persisted since the first edition, such as "Behind, the urethra is connected with the rectum." "The urethra has considerable extensibility, except the meatus, which must be cut," etc., that should have been corrected by now. One misses the exposition of the high-frequency treatment of chancroid, that has rid the clinic of much tedious work; nor can we agree that hexamethylenamin is "especially useful in the alkaline forms of chronic

cystitis," knowing full well that it is inert except in an acid urine. Small errors and oversights such as these mar the value of an otherwise excellent text-book (errors that should disappear in a third edition), and make one hesitate in recommending it without reservations. A. R.

POLYCYTHEMIA, ERYTHROCYTOSIS AND ERYTHREMIA (VAQUEZ-OSLER DISEASE). By F. PARKES WEBER, M.A., M.D., F.R.C.P. (LONDON). Pp. 148. London: H. K. Lewis & Co., 1921.

THIS timely book by a well-known London authority presents in 60 pages, a revised and expanded form of his critical review of this subject in the *Quarterly Journal of Medicine* for October, 1908. Case reports, notes on the more recent literature and on unpublished cases, together with a good bibliography, make up the rest of the volume. By a curious arrangement the bibliography only includes references not given in full in the text. Parkes Weber draws a sharp and useful distinction between absolute and relative polycythemia, the latter being due to greater concentration of the blood, the former to an increase in the total number of red blood corpuscles in the body. If absolute, polycythemia may be either primary (erythremia) or secondary (erythrocytosis). The latter form is shown in Part 1 to be chiefly due to high altitude or to imperfect oxygenation in congenital or chronic cardiac and pulmonary diseases. In Part 2 primary polycythemia (erythremia, splenomegalic polycythemia rubra, Vaquez-Osler disease, etc.) is presented in the most adequate form known to the reviewer. The author's belief that erythremia is a primary hyperplastic disease of the bone marrow, though open to the objection that it is little more than another way of confessing our ignorance, certainly seems the most logical in the present state of our knowledge. While further studies like those contained in this book may not in the near future be able to demonstrate the cause of erythremia, they should at least greatly reduce the number of cases now being included under this heading. E. B. K.

ANXIETY HYSTERIA: MODERN VIEWS ON SOME NEUROSES. By C. H. L. RIXON, M.D., M.R.C.S., and D. MATTHEW, M.C., M.B., CH.B. Pp. 120. New York City: Paul B. Hoeber, 1921.

IN 120 pages the authors discuss anxiety hysteria. They recognize three psychoneuroses: (1) anxiety hysteria (including conversion hysteria); (2) neurasthenia and (3) psychasthenia.

In the book only the first is dealt with. By the term anxiety hysteria the authors mean "that condition which is most usually

characterized by a certain anxiety type of facies, headache, insomnia, nightmares and frequently tremor, which symptoms are not dependent upon any organic disease of the central nervous system. It is frequently designated 'neurasthenia' but by the latter term "a condition which is etiologically and pathologically different is herein implied."

Their method of treatment can be summed up in the preface: "While we believe that these psychoneuroses must be met on their own ground and are best dealt with by psychological methods, and while for the most part analytical methods are employed by us, we wish it to be understood that we do not accept all the views propounded by Professor Freud and his followers. We are unable to believe that there is any sexual basis underlying the vast majority of these psychoneuroses, at any rate in military patients; and we hold the view that the emotion of fear is the causal agent at the bottom of ninety-nine out of every hundred such cases. Since, in the minds of the majority of medical men, the term 'psychoanalysis' is inseparably associated with these sexual views, we have altogether eschewed it. In its place we now employ that of 'mental exploration,' a term which is free from those implications, and which was originally devised, on that account we believe, by Professor C. S. Myers. Although we have written what follows mainly with reference to war cases, exactly parallel conditions obtain in civilian patients."

This is one of many books resulting from war experience with so-called shell-shock patients. The only excuse for the book, as stated in the foreword of Dr. A. Lisle Webb, is that it is "written in a way which shall be intelligible to the medical man who has no intimate knowledge of modern psychology and no special experience of psychotherapy."

The method of treatment is essentially psychoanalytic. It is too brief to be of value to the medical man who has no intimate knowledge of the subject and not large enough for the neurologist who wishes to learn more. T. H. W.

A Manual of Midwifery for Students and Practitioners. By Henry Jellet, B.A., M.D. (Dub.), F.R.C.P.I., L.M., late King's Professor of Midwifery in the School of Physic of Trinity College, Dublin, and David G. Madill, B.A., M.D., B.Ch., B.A.O. (Dub.), L.M., Gynecologist to Monkston Hospital, Dublin. Third edition. Pp. 1168; 20 plates; 570 illustrations. New York: William Wood & Company, 1921.

After a lapse of eleven years this excellent text-book by a former Master of the Rotunda Hospital has been entirely revised and

extensively rewritten. A perusal of the table of contents and the index gives an idea of the completeness of the book which is more than substantiated by a reading of the text. The subject-matter, divided into various sections, deals in a logical manner with the different phases of reproduction, pregnancy, labor, the puerperium, the surgery of obstetrics and the newborn. The section on the toxemias brings out full references to, and discussion of, all recent advances in the treatment of hyperemesis gravidarum, and eclampsia. The authors recommend and practice packing and version for placenta previa, although such other methods of treatment as extra-ovular insertion of rubber bags and Cesarean section for certain selected cases of previas are not condemned. There is an excellent paragraph on pituitrin. The subject of obstetric surgery is gone into fully. One particularly likes the care with which the details of operative procedures are brought out and described. Evidently these Irish authors are conservative in their ideas of obstetric surgery; version for every woman in labor as a time-saving device and the so-called prophylactic forceps operations are not considered in the revision. The volume may be highly recommended as an excellent text on obstetrics. P. F. W.

Ephraim McDowell, "Father of Ovariotomy" and Founder of Abdominal Surgery; With an Appendix on Jane Crawford. By August Schachner, M.D., F.A.C.S., Louisville, Ky. Pp. 331; 21 illustrations. Philadelphia and London: J. B. Lippincott Co., 1921.

The volume under consideration is a fairly complete exposition of Ephraim McDowell, his life, his surroundings, his confrères and opponents and, of course, his epoch-making work. Of his work the author states: "He placed in the diadem of the art and science of surgery its most brilliant gem and in the eons of time becomes the indirect emancipator of countless millions of human beings from protracted suffering and premature deaths. But after all this priceless service he practically remains unknown and unhonored." The purpose of the book is to acquaint the profession with the difficulties under which he worked and to correct some false impressions concerning him which have been accepted. For example, the traditional story that he was seriously threatened by a mob while performing the operation is based more upon fiction that upon facts. The most interesting part of the book is naturally the part dealing with the first operations, not only from the standpoint of originality, but because it gives the reader a keen insight into surgical practises and equipment of those early days. A section of the book is devoted to Jane Todd Crawford, who played the heroine's part in the memo-

rable "experiment." The author is to be congratulated upon the thoroughness of his work and we presume that the repetitions which have occurred were almost unavoidable. The publishers likewise are to be commended upon the beautiful style in which they have presented the volume. It should be a welcome addition to any medical library. F. B. B.

AIDS TO OPERATIVE SURGERY. By H. C. ORRIN, O.B.E., F.R.C.S. Ed., Surgeon, M. of P., Orthopedic Hospital, etc. Pp. 236. New York: William Wood & Company, 1921.

THIS work attempts to present to the student an epitome restricted to the salient features and essential facts of surgical operations. It is not a substitute for the classical text-books, but merely a compend useful to students in preparation for examinations. Each operation is dealt with in the briefest manner possible and only the absolute essentials are given, yet no step has been omitted, each being detailed in the order of its performance in the actual operation itself. Operative technic is not described nor are alternative methods of performing an operation always detailed. Yet the ground covered has been most extensive and the little book bears an important part in a student's library. E. L. E.

TEXT-BOOK OF EMBRYOLOGY. By FREDERICK RANDOLPH BAILEY, A.M., M.D., formerly Adjunct Professor of Histology and Embryology, College of Physicians and Surgeons (Medical Department of Columbia University) and ADAM MARION MILLER, A.M., Professor of Anatomy, The Long Island College Hospital. Fourth edition. Pp. 624; 503 illustrations. New York: William Wood & Company, 1921.

THE present revision of this standard text-book has been thorough and includes some changes in the make up of the book. Thus the early processes of development—cleavage, gastrulation and mesoderm formation—are no longer considered separately as such but grouped under the particular animal type, a modification which it is believed will facilitate the presentation of the subject to the student. The second part of the book, on organogenesis, includes a new chapter on fetal membranes and an interesting chapter on teratogenesis. The book is well gotten up, has a very complete index, is copiously illustrated, the photographic reproductions being very good. A good feature of the book is a well-selected bibliography at the end of each chapter. This revision gives a well-balanced description of the developmental processes in the human, and may be well recommended. P. F. W.

CLINICAL SURGICAL DIAGNOSIS. By F. DE QUERVAIN, Professor of Surgery and Director of the Surgical Clinic at the University of Berne. Third English edition. Translated from the seventh edition by J. SNOWMAN, M. D. Pp. 884; 731 illustrations and 7 plates. New York: William Wood & Company, 1921.

MANY English editions of foreign works in medicine suffer from a lack of adaptability in transposing idiomatic phraseology from one language to the other. The pleasing style and ease in reading of the volume in hand are due to the excellence of the translation, in which the vividness of the author's description suffers no loss.

This third English edition is derived from the seventh original edition. In it there has been added during the revision all new diagnostic points in the surgery of civil practice, and it reflects, also, the many advances in surgery gained by experience in the World War. Over one hundred new illustrations and plates, almost all original and excellent photographic reproductions, have been added. The book follows the former plan, taking up regional surgery, one part after another. Dealing first in the abstract with the morbid conditions of an organ, the author takes up concrete cases in sequence, turning his diagnostic reflections upon them to illustrate a point in question. A characteristic personal note, due to the author's large clinical experience, tinctures the discussion throughout the text. The book is warmly commended as an aid in surgical practice. P. F. W.

SURGICAL ANATOMY. By WM. FRANCIS CAMPBELL, A.B., M.D., Surgeon-in-Chief, at Trinity Hospital, Brooklyn, N. Y. Third edition, revised. Pp. 681; 325 original illustrations. Philadelphia: W. B. Saunders Company, 1921.

IT is the author's purpose to present anatomical facts in terms of their clinical values. Such a presentation is of distinct value to the student, and should be made use of, as soon as he has become acquainted with any region of the body by dissection. Emphasis is laid upon the normal functions of many of the parts described, and of their deranged functions following accident or disease. Thus in many respects such a book is a physiological anatomy. The author states that only those structures and regions have been emphasized which have a peculiar interest for the surgeon. A glance through the text and index shows how wide his interest is, for practically every organ and region comes up for consideration, with the exception of the pineal body and the coccygeal gland. This completeness is made possible by using short descriptions of structures and by the introduction of many diagrams. Such a commentary on human anatomy must be helpful to all those who are well grounded in the descriptive side of the subject. W. H. F. A.

COLLECTED PAPERS OF THE MAYO CLINIC, ROCHESTER, MINN. Octavo. Pp. 1391; 446 illustrations. Philadelphia and London: W. B. Saunders Company.

PAPERS from this clinic need no introduction and no recommendation other than their true title. This collection is especially good and, as usual, contributes a most wide-reaching scope of medical and surgical subjects. The greater number of the authors are writers of widely known reputations and upon whose statements we can depend and place the utmost confidence.

It is useless to single out individual contributions for reference or description. Suffice it to say that the volume holds a most wonderful supply of up-to-date scientific information presented admirably as in the past numbers of this same clinic. E. L. E.

ESSENTIALS OF LABORATORY DIAGNOSIS; DESIGNED FOR STUDENTS AND PRACTITIONERS. By F. A. FAUGHT, M.D. Seventh edition. Pp. 523; 11 full-page plates and 78 text engravings. Philadelphia: F. A. Davis Company, 1921.

SEVEN editions of this manual since 1909 are sufficient indication of its popularity with the medical public, and it undoubtedly presents valuable information, especially in the author's chosen field of blood-pressure. Even here, however, one regrets the absence of any consideration of venous pressure, or of Hooker's recent introduction of the capillary blood-pressure into the field of clinical medicine. The section on Clinical Hematology afforded the reviewer the most pleasure, which would have been even greater if a description of reticulocytes and of the resistance of erythrocytes to the usual hemolytic agents had been included. The section on the Sputum is inferior to the more complete original to be found in Bowditch's translation of Sahli's *Diagnostic Methods*. When such extensive adoption of text is made, a different form of acknowledgment would seem preferable. Typographical errors are few; on page 17, the Greek letter P should be replaced by μ as a symbol for a micron. E. B. K.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Observations on the Circulation and Respiration in a Case of Paroxysmal Tachycardia.—BARCROFT, BOCK and ROUGHTON (*Heart*, 1921, **9**, 7) determined the minute volume of the blood flow in a young man during attacks of paroxysmal tachycardia and during periods of normal cardiac mechanism. The subject was in apparent good health except for recurrent attacks of paroxysmal tachycardia, characterized by sudden onset and offset, shortness of breath, abnormal heart action, cyanosis, gastric disturbance, sweating and weakness. The method of determining the minute volume was that described by Barcroft and Roughton at the meeting of the Physiological Society in July, 1920 (*Jour. Physiol.*, 1920, **15**), using the formula:

$$\text{Minute volume} = \frac{O}{A = V}$$

when O = total oxygen used by the subject per minute, A = oxygen content of the arterial blood, and V = oxygen content of the mixed venous blood. With a normal cardiac mechanism and a pulse-rate of 64 the minute volume was 5 liters and the output of the heart per beat, 77.5 cc. During an attack, with a pulse-rate of 198, the minute volume was 2.5 liters and the output of the heart per beat, 12.9 cc. During the attack, also, the oxygen consumption was reduced and the total ventilation, in spite of tachypnea, was diminished. The venous blood showed a high degree of unsaturation; the saturation of the arterial blood, on the other hand, was, if anything, increased.

Paroxysmal tachycardia, then, presents a clear case of anoxemia of the stagnant or ischemic type, which in this case is pushed so far as to cause a reduction in the quantity of oxygen used, *i. e.*, "a crippling of the metabolism."

Studies on the Pneumonic Exudate. V. *The Relation of Pneumonic Lung Protease Activity to Hydrogen Ion Concentration, and a Consideration of the Origin of the Enzyme.*—NYE (*Jour. Exp. Med.*, 1922, **35**, 153), continuing the studies that he and LORD have been making on the pneumonic exudate (*Jour. Exp. Med.*, 1921, **34**, 199), points out the following facts: As early as 1877 it was demonstrated that leukocytes contain an enzyme or enzymes capable of splitting native proteins to simpler nitrogenous compounds. Opie, in 1906, working experimentally on sterile exudate, showed that there were two distinct proteolytic enzymes present, one derived from the polymorphonuclear leukocytes and acting best in slightly alkaline media, and one derived from mononuclear cells and acting best in slightly acid media. In the early articles it was shown that one enzyme in the pneumonic lung exudate acted best between pH 6.7 and 7.3, and another between 5.2 and 6.3, and the authors formulated the hypothesis that during the course of the disease in the pneumonic lung there is a gradual decrease in pH or increase in acidity. Primarily and at that time when the reaction of the exudate is about that of the circulating blood (pH 7.3 to 7.5) there is a digestion of the more highly organized proteins (fibrin, serum albumen, etc.) following the liberation of enzyme through cellular disintegration. With subsequent increase in acidity (beyond pH 6.7) the activity of this protease diminishes and conditions reach an optimum for the activity of the peptone-splitting enzyme. This peptonase or ereptase carries the splitting of the digestion products to amino-acids, absorbable as such; and resolution takes place. In this study Nye uses fibrin from the blood of horses and cellular suspensions from the consolidated lung. Since normal lung contains some enzyme it was necessary to rule out the action of this. The results show that there is present in the pneumonic lung an enzyme or enzymes capable of digesting horse fibrin which shows the maximum digestion (46 per cent of the fibrin) at pH 8 and the most complete digestion at pH 7. Normal lungs contain an enzyme which is active in a moderately acid medium, pH 4, and essentially inactive in less acid, neutral, and slightly alkaline medium. The possibility of the enzyme coming from pneumococci, cells normally present in lungs, or blood serum, is ruled out. He concludes that the enzyme is derived chiefly from the leukocytes, and is most active in a slightly alkaline medium (pH 8).

A Study of the Relation of the Adrenal Glands to Experimentally Produced Hypotension (Shock); with a Note on the Protective Effect of Preliminary Anesthesia.—RICH (*Bull. Johns Hopkins Hospital*, 1922, **33**, 79) found that the observations hitherto published regarding the relation of the adrenal glands to surgical shock were confusing and not infrequently contradictory to each other. The author carried out a series of nicely controlled experiments upon cats, some of which he subjected to adrenalectomy and subsequent intestinal manipulation, and others of which (ten in all) he subjected to identical operative

procedures and manipulation without previous adrenalectomy. Adrenalectomized animals fell into shock precisely as did the normal controls. It was also found that hypotension invariably followed removal of the adrenals before marked indications of asthenia supervened. The experiments prove conclusively that shock is not due to the elaboration of toxic material by the adrenals, since shock occurred equally well in the absence of these glands as in their presence. It seems, therefore, that the only tenable hypothesis by which the adrenals might be linked with shock would be to assume that the operative conditions were such as to completely overwhelm the organism and to render negligible any protective action which the adrenals might exert against shock. The author's conclusion that adrenal dysfunction is not a factor in the production of shock is a difficult one to escape. We should probably not, however, carry the dissociation of adrenals and shock too far. The author has stated that hypotension is one of the essential criteria of shock. He also concludes that the adrenals are a potent factor in the support of normal blood-pressure, since there is invariable hypotension following adrenalectomy. It seems, therefore, fair to conclude that, while adrenal dysfunction does not cause shock in the experiments carried out by the author, yet the fact that adrenal function supports blood-pressure is sufficient to place the adrenals upon the side of those factors that try, however ineffectually at times, to protect the organism from blood-pressure lowering agents.

A New Test of Hepatic Function.—HATIEGAN (*Bull. de l' Acad. de méd.*, 1922, **87**, 170), with the aid of the duodenal tube, has studied the elimination of various coloring matters by the liver and regards the indigo-carmine of Voelker as a peculiarly suitable dye for the purpose inasmuch as its appearance is rapid and its elimination of short duration. If injected in doses of 0.16 gm. its excretion is appreciable in about twenty minutes by a grass-green color of bile; this color becomes accentuated and attains its maximum two or three hours after its injection, when its intensity begins to diminish, until after five or six hours it reaches about the same shade which it had attained in the first forty or sixty minutes. In the normal liver, elimination begins after twenty minutes and reaches its maximum in two or three hours. In portal cirrhosis without icterus, 0.16 gm. is not always followed by an appreciable elimination. If the dose, however, is not under 0.24 gm. its elimination may always be made out, but the onset and the rhythm of the elimination are interfered with. In the first hour the bile is unaltered. After an hour the discoloration begins, reaching its maximum in from three to four hours. In five cases of portal cirrhosis without jaundice examined by the writer—cases which resembled one another clinically—the course of the elimination was essentially the same and indicated a delay explicable perhaps by the retardation of the hepatic circulation. The excretion, however, was of the same intensity as normally, but the period of elimination was delayed. A similar delay was observed in a case of cardiac failure. The writer concludes that "indigo-carmine" is eliminated by the normal liver and even by the diseased liver if there be no jaundice. This proceeding may be utilized for the examination of the excretory functions of the liver cell and the permeability of the

bile passages if the cellular excretory function be normal—a circumstance which authorized us in suggesting the employment of this procedure for the examination of hepatic affections in general. The dose necessary for an elimination is 0.16 gm.; to attain the reaction with certainty one must employ a dose of 0.24 gm.

Observations Relating to the Action of Quinidine Upon the Dog's Heart; with Special Reference to its Action on Clinical Fibrillation of the Auricles.—Lewis, Drury, Iliescu and Wedd, (*Heart*, 1921, **9**, 21), working upon dogs, were able to confirm previous work showing that quinidine causes (1) lowering of the rate of the sinoauricular rhythm; (2) slowing of the auricular-ventricular conduction; (3) slowing of the intraventricular conduction as shown by the increase in the length of the Q. R. S. group. They point out for the first time that conduction in the auricular muscle is also profoundly slowed. In an attempt to analyze the "lowered excitability" which has been noted by many workers, Lewis observed that quinidine in the doses used lengthens the absolute refractory period. Finally, a paretic action on the vagi has been observed. In the light of these known actions of quinidine, the effects of quinidine sulphate upon clinical fibrillation of the auricle are explained, if the last is regarded as fundamentally due to circus movement. "A sufficient lengthening of the refractory period, by reducing the responsive gap, will either bring the circus movement to an end or it will slow the circuit movements. A reduced rate of conduction will slow the circuit movements, but will tend to establish the circus movement more firmly. If the refractory period factor predominates, the circus movement will end; if the conduction factor predominates, the circus movement will not end, but will become slower. An increased rate of ventricular beating under quinidine, in auricular fibrillation, is ascribed to the lowered rate of auricular beating in part, and paresis of the vagi in part."

Hyperpermeability of the Liver in Diabetes.—Hatiegan (*Bull. de l'Acad. de méd.*, 1922, **87**, 236) pursuing his studies on the elimination of indigo-carmine by the liver, has observed, in a case of diabetes, a remarkably abundant elimination of this substance, so great indeed that with 0.24 gm. the duodenal content was of a blue color identical with that of the injected solution. The foam even of the duodenal juice was of an intense bluish color, a phenomenon which he had never observed previously. In six cases of diabetes mellitus 0.08 gm. of indigo-carmine—a dose so small that its elimination is not appreciable in the normal liver—was excreted in such quantities as easily to be demonstrable. In one of these cases 0.04 gm. indigo-carmine was excreted in quantities easily recognizable—the elimination following the normal course and rhythm. The writer believes that these observations prove that in diabetes the liver has undergone profound alterations which result in a hyperpermeability in regard to coloring matters. He believes that the hyperpermeability as well as the hyperabuminosis of the bile suggests that the liver has undergone grave functional alterations and has become a simple "filter." He regards these observations as supporting Glénard's well-known contention that alterations in the liver play a serious role in diabetes. His

cases were apparently all instances of severe diabetes; he refers to them as *diabète consomptif*. Two instances of mild diabetes showed no change. The writer believes that the indigo-carmine test may be of some value as a means of diagnosis between milder and severer forms of diabetes.

SURGERY

UNDER THE CHARGE OF

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The Results of Ninety-eight Cases of Nerve Suture.—DARE (*British Med. Jour.*, June 18, 1921, p. 885) says that all his cases are the result of gunshot wounds and have been under observation from twelve to thirty-six months. The author has taken the amount of motor recovery as the standard because it is more important functionally and was more easily determined. Sensory recovery, however, was more complete and earlier than return of motor power. Good or satisfactory results were obtained in 51 per cent of the cases, while 49 per cent were bad results. The series included ulnar, median, musculospiral, sciatic, musculocutaneous and brachial plexus lesions. The only cases to receive any preoperative or postoperative treatment by means of splints were a few of the musculospiral cases. The author feels that 51 per cent greatly exceeds the real truth, especially if one regards recovery from the point of functional usefulness. The results, on the whole, then are in some measure disappointing, considering the tremendous amount of regenerative power that the axis cylinders possess—probably more than any other tissue in the body. The neglect of splints has been responsible for most of the failures, especially with regard to the delicate intrinsic muscles of the hand. Electrical methods have not impressed the author and in the future he will not employ them for it is impossible to know exactly what one is doing in many cases. Moreover, Scheft showed, in 1851 (Langley confirmed his results in 1916), that a denervated muscle is in a state of fibrillation. The keynote of treatment is rest with gradual reëducation to muscles that have been injured by denervation from whatever cause. The recovery of sensation is practically never perfect, but in a great many cases some recovery of sensation returns and this of itself is a great advantage to the individual, protecting him from burns and other injuries and also indirectly leading to an increase of nutritional activity.

The Treatment of Syphilis by Intravenous Injections of Mercury.—LANE (*Lancet*, October 15, 1921, p. 796) says that this treatment was more rapid in its effect than any other method of mercurial adminis-

tration, painless in comparison with intramuscular injections and perfectly safe. One per cent solution of cyanide of mercury was employed and the dosage varied with the tolerance of the patient. It was found that many patients could stand 40 to 50 minims as a dose which was given five times a week. The maximum number of injections was 110 for a very severe framboesiform syphilide, while the average number ran a little over 40. The strictest attention was paid to hygiene of the mouth and the occurrence of severe gingivitis was rare. Routinely one injection of salvarsan substitute was administered weekly.

The Accuracy of the Formalin and Sachs-Georgi Tests for Syphilis.—KINGSBURY (*Lancet*, October 15, 1921, p. 799) says that the accidental discovery in 1920, by Gate and Papacostas, that the addition of a small quantity of formalin to pooled syphilitic serums produced coagulation, and was without effect on normal serums, forms the basis of this new test. The results obtained from the formalin test prove once again the futility of basing conclusions on figures derived from a small number of cases, as small series have recently been published showing complete accord between formalin and Wassermann reactions. The technic of the test is simple and if the results were reliable it would be an excellent method whereby the practitioner could establish a diagnosis of syphilis. But less than half of the serums giving positive Wassermann reactions showed coagulation with formalin and—a fact of greater importance—nearly 10 per cent of non-syphilitic serums give a positive result. Any claim to the reliability of the test is, therefore, demolished. As early as 1910 it was pointed out that extracts of various organs gave a slight precipitate when added to syphilitic serum. The precipitate was found to be inconstant and was considered to be of little diagnostic value. In 1918 Sachs and Georgi called attention to the fact that the addition of a solution of cholesterol to alcoholic heart extract made a good antigen for a precipitation test. The results obtained are distinctly promising. The technic is much simpler than that of the Wassermann reaction, but there is great difficulty in determining the presence or absence of a precipitate in many instances. A strongly positive Sachs-Georgi reaction may be taken as evidence of syphilis, but a weak reaction must be looked upon with suspicion because of the difficulty in distinguishing between the weakest positive reaction and the slight precipitation given by some negative serums. The detection of the weakest positives may, however, be made easier by modification of the antigen and by special methods of reading the results.

The Indications for Surgical Treatment in the Different Types of Goiter.—SISTRUNK (*Surg., Gyn. and Obstet.*, 1921, **33**, 348) says that there are only three types of goiter—colloid, adenomatous and exophthalmic. Other types seen clinically are either variations or combinations of these three. Colloid goiter is definitely a goiter of youth and is the only goiter which disappears under the administration of iodine or thyroxin. The adenomatous type is the most common; 23 per cent of the patients with this type seen in the Mayo Clinic show symptoms of hyperthyroidism, but these symptoms do not develop until

the goiter has been present for an average of sixteen years. In young persons, unless the goiters attain considerable size or produce symptoms of pressure, they are not considered surgical. In the majority of instances after patients with adenomatous goiter have attained the age of twenty-five years surgery is advocated. All goiters of this type associated with hyperthyroidism are considered surgical if the condition of the patient will permit an operation. Exophthalmic goiters occur at any age but most often between the ages of twenty and forty. The condition is best treated surgically and the best results are obtained in patients operated on early in the course of the disease before marked damage has been done to the vital organs. Many patients require one or two ligations of the superior thyroid vessels preliminary to thyroidectomy in order to make it a safer procedure. If care is exercised in selecting the type of operation for a given case the mortality is low.

Clinical and Experimental Observations in the Use of Saline Irrigation in the Treatment of Diffuse Peritonitis.—Willis (*Surg., Gyn. and Obstet.*, 1921, **33**, 553) says that Murphy and others object to saline irrigation in diffuse peritoneal infection because it tends to produce shock by subjecting the patient to a longer operation, traumatizing the peritoneum and accelerating absorption, while washing off the defensive phagocytes. In favor of free irrigation it may be said that it lessens tendency to shock by prevention of undue loss of body heat. Moreover, it washes out mechanically unabsorbed bacteria, fibrin, pus, blood clots and intestinal contents which may serve as foreign material, facilitating the growth of bacteria. Finally, the peritoneum is an absorbing surface of greatest activity. Ruptured appendix, or appendiceal abscess, is a very frequent cause of fatal peritonitis. The author has had 1034 cases of acute appendicitis in the past twelve years; 33 cases were considered instances of true perforative diffuse peritonitis—some 3 per cent. Fortunately, for purposes of analysis his cases could be divided into two series—the earlier 14 in a period of five years were operated by the principle of rapid operation with minimal abdominal manipulation. The mortality was 50 per cent. The later series was made up of 19 patients, 18 of whom were treated by free incision, the opening of all pockets and combined irrigation with normal saline and the use of a water or electric suction apparatus. The mortality was 16 per cent. The author feels that a shorter and smoother convalescence is gained by this procedure. Of course gastric lavage, opiates and free use of salt solution per rectum and subcutaneously were employed in both series.

Further Data Concerning the Experimental Production of Pancreatitis.—Archibald and Gibbons (*Ann. Surg.*, 1921, **70**, 426) say that there are three principal theories: (1) The pancreatic lesion is caused by the entrance of bile into the pancreatic duct by reason of an obstruction at the outlet of the common duct; (2) the lesion is caused by an infection travelling from an inflamed gall-bladder to the head of the pancreas by the lymphatic route; (3) that duodenal contents are forced into the common duct through the ampulla, and so into the pancreatic duct. Infected bile aspirated from the inflamed gall-

bladder exercises a much more severe necrosing and inflammatory effect upon the pancreas than does normal bile. Chemical investigation of infected bile has not yet proved that this difference of effect is due to an increase in concentration of the bile salts as the result of bacterial action on the bile. Mild grades of pancreatic swelling as estimated clinically are certainly possible and are represented by edema with early necrosis of the parenchyma, presumably the result of bile invasion. The clinical statement in operation records as to the presence of "a somewhat thickened and indurated pancreas" is probably a correct interpretation of fact in most cases. The gall-bladder, under conditions of irritation from stone or inflammation, is probably able to go into strong muscular contraction and the hypothesis is set up that such contractions may provide sufficient driving force to cause invasion of the pancreas with bile. The common duct sphincter is provoked to resistance not only by the acidity of the duodenal contents but also by sudden distention of the common duct through unexpected rises of pressure in the gall-bladder.

Surgical Management of Gastric Ulcers.—BALFOUR (*Ann. Surg.*, 1921, **74**, 449) says infectious foci should be systematically searched for while postoperative direction of diet and habit of living should be included in present surgical management. The selection of operation is of great immediate importance and it is very probable that further progress will come from intelligent selection and application of methods now known rather than from additional operative methods. Four main considerations upon which the value of any operation for gastric ulcer should be judged are simplicity, applicability, immediate results and ultimate results. The author finds in the study of the Mayo Clinic cases that gastroenterostomy with cautery excision of the ulcer surpasses other methods by these standards. Gastro-jejunal ulcer is not wholly a sequel or complication of gastroenterostomy. Ulcers occasionally recur and new ulcers also form sometimes after any type of gastric operation. The author believes that the routine eradication of all septic foci and the adoption of a proper postoperative dietary and therapeutic regimen will be the greatest advance in preventing these recurrences. In the question of protection against cancerous degeneration the problem is unsettled. There is one fact certain—that no operation for gastric ulcer will absolutely assure a patient that he will not die of gastric cancer.

Arthroplasty.—PUTTI (*Jour. Ortho. Surg.*, 1921, **19**, 421) says that the modern methods of arthroplasty allow us to create articulations that can attain functional properties which in some cases are equal to those belonging to normal joints. In others the new joint can fully satisfy the most exacting wishes of the patient. These articulations are able to support for many years even the work of trades which are very fatiguing. Some of the author's patients operated on for arthroplasty of the knee and elbow have been declared capable for military service in the late war. In ankylosis of the lower limb it is possible to obtain articulations which are not only quite moveable but also able to support the greatest fatigue. The progress in the field of arthroplasty is due to the interposition method. The author makes free flaps of fascia lata his choice.

OBSTETRICS

UNDER THE CHARGE OF

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Uteroplacental Apoplexy and Accidental Hemorrhage.—WILLSON (*Surg., Gyn. and Obst.*, January, 1922) reports the case of a patient of unknown history admitted to hospital with albuminuria and edema. The fundus was three fingers' breadth above the umbilicus; the position of the fetus was transverse; the fetal heart was heard in the right lower quadrant and the pelvic measurements were slightly less than the average. Under appropriate treatment the albuminuria disappeared. Labor began with severe pains, and continued for about two hours when bleeding occurred from the vagina with nausea and vomiting. There was great pain and tenderness in the abdomen with prostration. The patient apparently had developed severe shock and considerable bleeding from the vagina. The abdomen was very tender; the uterus tense and hard without relaxation; palpation of the fetus was impossible, but the head was at the brim; the heart could not be heard. On vaginal examination the cervix admitted one finger, and no placental tissue could be found. Diagnosis was made of premature separation of the placenta. At operation there was considerable blood-stained serum in the peritoneal cavity. The uterus was mottled bluish, almost black in color, and the discoloration was greatest in the region of the left cornua. Both anterior and posterior walls of the uterus were involved. There were fissures in the uterine wall, running parallel with its axis. The peritoneum had not been torn through; the tubes and ovaries were apparently normal. On opening the uterus the placenta was on the left side of the anterior uterine wall and one-third separated. The uterus contained over a quart of fluid and clotted blood. The fetus was dead and was removed in its membranes. The uterus was not removed but closed and left, and salt solution was given under the skin. The patient died three hours after operation. At autopsy the liver was pale and softer than usual; the gall-bladder normal; the spleen soft; the stomach and intestines apparently normal. The kidneys were pale and softer than the average; the tubes and ovaries normal, while the uterus showed subperitoneal hemorrhages over its entire surface and in the broad ligament on the side. The wall of the uterus was very soft and the muscle fibers were separated by considerable spaces. There was a central necrosis of the liver lobules, showing slight pigmentation and slight fatty degeneration. There was also an acute degeneration in the kidneys and in the muscle of the uterus. There were marked hemorrhagic extravasations between the bundles of muscle fibers. The placenta was apparently normal with the exception of a slight hyaline appearance in the stroma of the villi. The writer has collected reports of 69 cases including his own, and finds that, so far as causa-

tion is concerned, the mechanical theory of distention of the uterus, the forcing of blood into the uterine wall and obstruction to the outflow of the blood from the uterus fail to account for all of the conditions. The weight of opinion tends to the belief that toxemia is the most important factor in causation. There is a striking similarity between the pathological picture, seen in these cases, and the results produced by the toxins of snake poisons. The frequent coincidence of eclampsia and accidental hemorrhage is familiar. Possibly increased blood-pressure, so common in both, may be a factor. The prognosis is always grave, and in 50 cases in which a diagnosis was made during life the mortality was 38 per cent; the fetal mortality was 92.5 per cent in 67 cases. While all cases of accidental hemorrhage are not necessarily fatal and may not require operation, in severe cases occurring before or early in labor immediate operation is demanded. This should always be abdominal Cesarean section. Every effort should be exhausted before the operator proceeds to remove the uterus. If, however, bleeding continues, supravaginal amputation should be done. The Porro operation is often indicated. Uteroplacental apoplexy is caused by the inundation of the uterine wall with a toxin, producing bleeding, liberated from the placenta and naturally producing its greatest effect at the placental site. Accidental hemorrhage in the great majority of cases is a manifestation of the same process. The damaged state of the uterine wall tends to cause both intra-abdominal and postpartum hemorrhage. Where the cervix is undilated and hemorrhage is severe abdominal Cesarean section with hysterectomy is indicated.

Treatment of Abortion Complicated by Fever.—HEBERER (*Zentralbl. f. Gynäk.*, 1921, p. 859) has studied cases of abortion complicated by fever by making a bacteriologic examination of the blood, the contents of the uterus and the placenta. Fifty cases were available for these studies. The results are of decided interest and show how complicated are the findings in bacteriologic cases and how much dependence must be placed on clinical symptoms alone. Within forty-eight hours after the occurrence of the abortion 42 of the patients (84 per cent having fever) were treated by the emptying of the uterus with operative means. These patients made a rapid convalescence without fever and were discharged in good condition in eight or nine days. The interesting part of this paper, which narrates minute and painstaking bacteriologic study, is the statement that one cannnot base treatment on the bacteriologic findings in these cases. One must plan his treatment entirely upon the clinical symptoms, including a very thorough and careful bimanual examination. The writer's experience causes him to believe that the best treatment for cases of abortion with fever is to clear out the uterine cavity at the earliest possible moment. HELLENDALL (*Zentralbl. f. Gynäk.*, 1921, p. 867) has tried to apply the use of Dakin's solution, as employed by surgeons during the war, to obstetric and gynecologic cases. In 6 cases of abortion complicated by fever, after the uterus had been thoroughly emptied by an injection of from 1 to 3 quarts of 0.5 per cent Dobert's solution there was a rapid fall of temperature. A similar result was obtained in a patient who had parametritis and hemorrhage after an abortion at the fifth month, and when the uterus had been emptied. In this case a midwife had

attempted to extract the placenta. The patient's condition greatly improved and in three days she was practically convalescent. In another case of abortion at three months with retained placenta and very offensive discharge, two quarts of Dobert's solution were used as an injection followed by the rapid decline of the temperature. There were 6 patients in whom the fetus had died at about the sixth month. In some of these cases the membranes had ruptured and in others they were unruptured; in some the cervix was dilated and in some it was closed. Some had fever without chills and others had chills and fever. These patients were treated with copious irrigation with 0.5 per cent Dobert's solution. In 2 patients the night after the injection was made the temperature rose very considerably and the patient had chills, but after this the temperature fell and the patient improved. In the other cases the use of the remedy was not followed by chills. Perhaps the most interesting result was obtained in the case of a patient who had fever during delivery. The attending physician had stated that the patient required Cesarean section and she had been in labor from four to twenty-four hours. The membranes had ruptured three days previously. A midwife in attendance had examined the patient repeatedly during each day. The attending physician had made an attempt to deliver by forceps. The patient's pulse was 124; her temperature 102.5° F. The os uteri was about two-thirds dilated. The true conjugate was 7.5 cm. and the fetal head was freely movable at the pelvic brim. After a delay of ten hours, during which the patient had pituitrin given three times, the head became fixed in the pelvic brim and the cervix more largely dilated. There was an episiotomy performed and a living child was extracted by the high application of the forceps. The placenta and the amniotic liquid had a very foul odor. After the uterus was emptied it was copiously irrigated with three quarts of Dobert's solution. During the first four days after delivery her temperature reached 102° F.; pulse 120, with very foul discharge from the uterus. After that the symptoms subsided and the patient did well.

GYNECOLOGY

UNDER THE CHARGE OF

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Radiation versus Surgery in the Treatment of Myomata.—The working rules that have been adopted by CROSSEN (*Jour. Missouri State Med. Assoc.*, 1922, **19**, 55) are that radium is the preferable form

of treatment in uncomplicated small and medium-sized myomata in patients in the menopause or near the end of the child-bearing period. Persistent bleeding is usually the serious symptom in these cases and this is promptly controlled by radium, which checks all bleeding, menstrual or otherwise. Nearly all properly selected cases prove amenable to this treatment. It is very important to exclude carcinoma of the endometrium by performing a diagnostic curettage before subjecting the patient to radium treatment. In patients with kidney, heart and other complications giving undue operative risk, radium may be reasonably tried in the somewhat larger growths, especially in those cases where roentgen-ray treatment produces such marked nausea and ill feeling that it is not advisable to continue it. The larger growths in patients presenting undue operative risk are best handled by deep roentgen-ray therapy. In most cases this will, after a time, stop the bleeding temporarily and give a chance to build up the patient for operation. If she cannot be gotten into condition for operation, continuation of the roentgen-ray treatment may stop the bleeding permanently and diminish pressure symptoms by shrinking the growth. If preferred, the smaller growths also may be treated by roentgen-ray instead of radium, with practically the same percentage of symptomatic cures. In over 600 reported cases of myoma treated by roentgen-ray the bleeding was stopped in approximately 95 per cent. However, the roentgen-ray treatment has the disadvantage of extending over a long period of time, or if given in more massive doses in a short period, of upsetting the patient's digestive and nervous systems, in some cases to a serious extent. Large growths, larger than a grapefruit, are best handled by operation. It is not practicable to fix an arbitrary limit of size as other complications have a bearing on the decision. For example, pedunculated subperitoneal growths are not so favorable for radiation as those embedded in the uterine wall and hence must more often be removed by operation. Again, a single large growth is not so favorable for non-operative treatment as a myomatous uterus enlarged to the same size by a number of small nodules. In young women, in whom preservation of the child-bearing function and of menstruation is desirable, myomectomy is the preferable form of treatment, where any serious treatment at all is necessary. In many of these cases the myomata may be removed without disturbing the functions of the uterus. However, a point to be kept in mind is that when the abdomen is opened it may be found necessary to sacrifice the uterus in order to remove the tumors completely, hence myomectomy should be advised only after careful consideration of all the features of the case. If the growths are not of a size and location necessarily interfering with pregnancy or labor, it would be well to try first to check the bleeding by other means, such as curettage and internal medication. If these measures fail, it may be advisable in exceptional cases to employ light doses of radium or roentgen-ray, with the idea of giving just enough to control abnormal bleeding but not enough to affect ovarian or uterine function seriously. But in spite of advances made in the regulation of the dosage and the enthusiastic assumptions of some authorities, the writer regards this as hazardous to the preservation of function and hence employs these measures for this purpose with very decided caution. If the roentgen

ray is used, it is preferable to apply it to one side only, so that one ovary will remain unaffected. In complicated cases, the complications often make operation advisable in a growth which if uncomplicated would be suitable for radium or roentgen-ray treatment. The complication may be inflammation of some adjacent structure, for example, appendicitis or salpingitis. Such associated trouble is found in a considerable proportion of the cases of myoma. It should be remembered that a myoma that begins to grow after the menopause is probably undergoing a degenerative change of some kind and should be promptly removed if the patient is a safe operative risk.

Treatment of Inoperable Cervical Cancer.—Anyone familiar with the subject will realize that there are more cervical cancers that are inoperable when first seen than there are cases suitable for the radical operation. Radium has been of inestimable value in the palliative treatment of the inoperable cases; but unfortunately radium is available to a comparatively small number of the profession, while the inoperable cases of cancer of the cervix are of necessity left to the care of practically all of the general practitioners, many of whom are at a loss to apply any treatment as a palliative. In view of these facts GELLHORN (*Jour. Missouri State Med. Assn.*, 1922, **19**, 59) calls attention to a method of treatment which he originated fifteen years ago and which he considers second only to radium in the suppression of the awful symptoms of inoperable cancer of the uterus. The technic is briefly this: The cancerous masses occupying the cervix are scraped or scooped out with a curette, or, better still, with a very large, sharp spoon. This may require a few whiffs of ether or chloroform, but in many cases a preliminary injection of morphine renders this short initial step painless. Do not lose time with attempts at checking the bleeding, which is usually abdundant, but raise the foot end of the examining or operating table and insert into the vagina a well-lubricated Ferguson or other tabular speculum. Pour into this speculum a tablespoonful of pure acetone, which will check the bleeding immediately. Lower the speculum after about ten minutes and permit the acetone and clotted blood to run out, and fill the speculum once more with pure acetone. The speculum is now held in place for about fifteen or twenty minutes, usually by the patient herself, after which time the table is lowered so that the fluid will run out of the speculum. The latter is now thoroughly washed out with cotton pledgets soaked in water and then withdrawn. No packing is left in the vagina. There is absolutely no pain connected with the procedure, provided that the acetone does not touch the vulva. Even a single drop of acetone upon the mucosa of the vulva would cause an intense burning, which, however, can be relieved at once by washing it off with water. It is for this reason that a tubular and not a bivalve speculum must be inserted, and that the amount of acetone used must not be so large as to run out and over the vulva. The treatment as outlined above is repeated every two days for at least three weeks, except that the curettage is omitted. Later the intervals between treatments are lengthened to three or four days, and as the condition responds to the applications, treatments are given only as the case requires. The beneficial effect of the treatment is usually very prompt. The hemorrhages are as a rule the

first to disappear. The discharge becomes more watery and soon loses its offensive odor. The general condition of the patient improves fairly rapidly as appetite and strength return, and the severe pain which had interfered with sleep usually decreases to such an extent that very small doses of opiates or even salicylates suffice. Gradually the crater in the vagina shrinks perceptibly and the patient regains, for a time at least, the feeling of good health. The writer has been able to prolong life in this manner with a certain degree of comfort in hundreds of cases, but in spite of such good results he still insists that radium is the best treatment of inoperable cancer of the cervix if it is obtainable, but where not obtainable the acetone treatment is the best substitute.

Results of Operations for Uterine Prolapse.—The results of operations for uterine prolapse, as reported in the literature, after careful follow-up investigation, have been rather disappointing to SPALDING (*Calif. State Jour. Med.*, 1922, **20**, 2), so he determined to investigate the results obtained in a series of 76 patients operated upon in the Stanford University School of Medicine. All of the patients in this series had cystocele and 68 had rectocele. The cervix was lacerated in 52 of the patients, eroded in 38 and hypertrophied in 52. The uterus was retroverted in 51 patients, was prolapsed to the vulva in 26, through the vulva in 16, and presented outside the vulva with cystocele and rectocele in 34 patients. The chief complaint with 59 patients was "falling of the womb," although 32 mentioned backache. In all but 1 case some type of perineorrhaphy was done, and in 6 of the more recent cases the rectum was supported by a more extensive proctopexy. In somewhat less than half, the cervix was repaired either by amputation or trachelorrhapy. 2 patients died from the operation and 13 could not be traced, while of the remaining 61 patients in the series, all but 8, or 87 per cent, were entirely cured of their original complaints. On 19 patients at some subsequent examination, it was possible to demonstrate some degree of recurrence, although many of these patients were relieved of their original complaints. 3 patients had decided prolapse of the uterus. The operations for these patients had not been well planned, inasmuch as the uterus, which reprolapsed after an interposition operation, was pathological and should have been removed, the patient being cured by a subsequent vaginal hysterectomy. In a second case, the interposing the cervix under the bladder after a subtotal vaginal hysterectomy was not successful, the patient later being cured by suspending the prolapsed cervix by laparotomy. Cystocele recurred with 9 patients, but this is an entirely preventable recurrence if the pelvic fascia is overlapped under the bladder. Rectocele recurred in over 22 per cent of the cases no matter what particular type of perineorraphy was done. As a result of his investigation the writer concludes that prolapse of the uterus can be cured with a very small degree of operative risk if the patients are carefully observed before operation to exclude other causes for cystitis and backache. Prolapse should recur only rarely after operation and cystocele never, provided infection can be excluded. Rectocele is more difficult to cure unless a high dissection of the posterior plane of the pelvic fascia is made and the rectum fixed to a point behind the cervix.

OPHTHALMOLOGY

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Treatment of Choked Disk by Excision of the Sheath of the Optic Nerve.—KUBIK (*Klin. Monats. f. Augenhk.*, June, 1921, p. 898) sets up the following indications for the treatment of choked disk appearing with symptoms of brain tumor or increased intracranial pressure. (1) All localizable and accessible brain tumors are to be subject to radical operation. (2) In cases of non-localizable brain tumors, including pseudo-tumors, palliative interference upon the skull is to be practised (trephining). (3) Müller's operation of excision of the sheath of the optic nerve is to be practised as the least dangerous operative inteference in all cases in which operation upon the brain is refused, and in cases of absence of any special etiology for the occurrence of the involvement of the papilla, when the neurological examination does not indicate a brain tumor; but even in these cases, where the seat of the effect can not be assumed to lie within the posterior portion of the skull, lumbar puncture is the operation of first choice. (4) Where the choked disk does not subside after a palliative operation, or the vision continues to deteriorate, early excision of the sheath should be superadded. In any event, the writer regards this operation as a valuable addition and deserving of extended application. Further experience should lead to greater precision in the indications.

Genesis of Myopia.—Probably no question in the entire range of ophthalmology has received greater attention than this of the origin of myopia. The subject is still a live one, as is evidenced by the discussion which is constantly reappearing in the literature. In this connection, HANSSEN (*Klin. Monats. f. Augenhk.*, August, September, 1921, p. 171) publishes the results of autopsy of a case of high myopia which, in his opinion, clearly shows the relation between the position of the myopic globe to that of the optic nerve in the orbit. In this case, as is well shown in an accompanying photograph, the enlarged globe was seen to extend backward with the nerve markedly curved in the shape of an S. This case, in his opinion, clearly demonstrates that the nerve not only exercises no traction upon the posterior pole, but that, on the contrary, the bulb exercises a force of compression backward upon the nerve. It may be of interest to give a short *resume* of the hypotheses as to the origin of myopia which assume some sort of traction between the globe and the nerve. Hasner supposed the optic nerve to be absolutely or relatively too short, so that during convergence the nerve caused traction upon the sclera in the region

of the posterior pole. Weiss favored the same view: According to him the free portion of the nerve between the foramen opticum and posterior surface of the sclera is too short. In 1908, Levinsohn emphasized the significance of the position of the head during near work; he assumed that upon bending forward of the head, the eyeball advanced through gravity and venous congestion; the optic nerve, fixed as it is, by connective tissue, bloodvessels and nerves, exercises a not unimportant drag upon the posterior pole and thus occasions the well-known myopic deformation; this writer attempted to establish his hypothesis by experiments upon animals. Finally, Dinger made exhaustive studies upon the influence of the position of the head upon that of the eye, and also of the shape and interior configuration of the same. He agrees with Levinsohn that from the forward sinking of the globe, traction must occur by the relatively shortened nerve; such traction, though slight, he regards as adequate in the developing eye of youth to result in enlargement at the posterior pole and lengthening of the axis.

Artificial Eyes.—Coulomb (*Archiv. d'ophtalmol.*, November, 1921, p. 677) urges the constant wearing of the newer forms of double-shelled prothesis, as against the former method of wearing the older models (simple shells). The latter offer, by means of their posterior concave wall, a lodgment for the tears, forming a veritable moist chamber which macerates the conjunctiva, such maceration causing irritation of the mucous membrane and the mucopurulent secretion, involving the unpleasant necessity of removing the shell during the night and frequently cleansing the orbit. With the double shells there is no space between the bottom of the ocular cavity and the posterior surface of the artificial eye; the tears circulate normally and carry away to the lacrimal drainage apparatus dust and other impurities; no cleansing lotions of any kind are required. To secure perfect tolerance, the shells must be perfect in finish and polish; imperfections hardly supported during waking under frequent winking, become insupportable at night when the lids are closed. The shell should be relatively small and a new one substituted when the first one loses its polish. These shells naturally do not last very long, being worn constantly—eight or ten months on an average. On the other hand, not having to be handled and frequently cleansed, there is little danger of accidental breakage.

Difference in Size of the Pupils; Homolateral Miosis from Parasympathetic Repercussion in Affections of the Head.—Lafon (*Annal. d'oculist.*, October, 1921, p. 736) concludes that unilateral affections of the head, traumatic or otherwise, may occasion an inequality of the pupils, in the form either of homolateral mydriasis or miosis. In the former case, the lesion, in general superficial, provokes an irritation of the centripetal fibers of the thorax lumbar sympathetic system which spreads to the bulbar pupillo-motor nucleus of the same system, resulting in dilatation of the pupil of the same side. In the second case (miosis), the lesion, in general profound, provokes an irritation of the centripetal fibers of the cranial para-sympathetic, or autonomous system, which likewise spreads to the meso-cephalic

pupillo-motor nucleus depending upon the same system, giving rise to a narrowing of the pupil of the same side. Such mydriasis and miosis, from repercussion, are accordingly of the spasmodic type. Beside their homolaterality, they possess characteristics in common of not directly altering the sensory-motor reactions, and of not being accompanied by other elements of the syndromes of excitation or paralysis of the cervical sympathetic or third nerve; such anisocoria becomes more marked in darkness, while it diminishes and tends to disappear in bright light.

Ocular Disturbances Complicating Otitis Media.—GURDIL (*Paris Thesis*, 1921) finds that the ocular complications occurring in the course of otitis media are paralysis of the sixth nerve (9 per cent) and papillary stasis, with or without neuritis, 60 per cent. The paralysis is encountered particularly in those cases of otitis with intracranial complications: The immediate causes are diverse: Foci of circumscribed meningitis, cerebellar abscess, thrombo-phlebitis. Cases have also been observed without intracranial complications; the pathogeny of these is difficult of explanation: In these, too, quite probably there is some affection bearing directly upon the nerve. The alterations of the optic nerve observed in the course of otitis, present themselves under two forms: Simple papillary stasis, unaccompanied by immediate signs of disturbance of function in cases where ventricular hypertension is alone present; stasis with neuritis and rapid failure of vision, when to the ventricular hypertension is added a meningeal infection along the sheath of the optic nerve. Systematic examination of the fundus in the course of otitis media accompanied by general symptoms will alone render possible the detection of such alterations of the optic nerve. Treatment depends upon early diagnosis; good results are obtained in papillary stasis particularly. Lumbar puncture will be of service in cases of slight hypertension; it must be repeated several times. In cases of hypertension with papillary stasis, recourse must be had to decompressive craniectomy; to be effective intervention must be made before the process has proceeded to atrophy. In stasis with neuritis, vaccino-therapy is of prime importance where it has been possible to isolate the infectious germ.

Inequality of the Pupils as an Early Sign of Pulmonary Tuberculosis.—The idea of the frequency of inequality of the pupils in pleuro-pulmonary affections is not a new one; it has been referred to during the past years by numerous writers. SERGENT (*Bull. de l'Acad. de méd.*, April 12, 1921) has made a study of the subject, especially in pleuritis of the apex; he has shown the importance and frequency of unilateral mydriasis from irritation of the sympathetic as a diagnostic mark of early lesions—at times preceding all other signs. The same writer has studied a latent inequality rendered manifest by instillation of a weak solution of atropin, 1 : 1000. Before making the test, it is necessary to make sure that the eye itself is free from disease. After instillation, the beginning of the reaction must be observed attentively; it commences in general after ten or twelve minutes, and increases progressively to become complete at the expiration of twenty to twenty-five minutes; one pupil begins to dilate before the

other, increases more rapidly to its maximum, and first loses the light reflex, following which equilibrium between the two pupils is reëstablished, both being completely and equally dilated during two or three days. In the reverse order, the healthy pupil returns to its normal condition first, while the other remains larger for a longer time. A detail of great importance is the instillation of the identical quantity of the solution in each eye. The writer sums up the results obtained by the following statistics: 10 cases without pulmonary lesion, test entirely negative; of 18 cases with confirmed unilateral pulmonary lesion, in 11 the pupil test was positive; in 3 cases of absence of pupillary inequality under atropine there was evidence of cicatricial lesions in the chest; in 23 cases with uncertain physical signs, in 15 the test was positive upon the side which had aroused suspicion upon auscultation; in 7 cases with inequality before instillation, the condition became more marked after atropine; in 1 case the inequality was reversed after instillation, but in this case there were bilateral lesions. The above results seem to establish the value of the test; in fact, they are confirmatory of results already obtained by Cantonnet in the same way. It thus appears that the test may render considerable service clinically in affording an additional diagnostic element in doubtful cases.

Tuberculous Dacryoadenitis.—Beauvieux and Pesme (*Archiv. d' ophtal.*, January, 1922, p. 22) conclude that tuberculosis of the lacrimal gland is an extremely rare affection. It occurs under two forms: Exceptionally as a caseous process, and more commonly as a sclerosis. It is found in patients with manifest tuberculosis, and again in youths or adults apparently free from all bacillary taint. The disease of the gland is of hematogenous origin, being secondary to some apparent lesion or else to an unrecognized deep focus of infection. The process is an attenuated one, little virulent; it is characterized pathologically by perivascular and periacinous infiltration of inflammatory cells accompanied by typical or atypical giant cells; scleratizing fibrous tissue predominates, forming a barrier to the infection and limiting the same to small circumscribed islets, in the midst of which normal or degenerated acini are visible; Koch's bacillus is almost uniformly absent. Attenuated tuberculosis of the lacrimal gland presents itself in the form of an indurated tumor with slightly irregular surface, mobile, painless, increasing slowly, and capable of spontaneous recession; it may be uni- or bilateral. The prognosis, so far as the local disease is concerned, is favorable; the general prognosis depends upon the degree of systemic tuberculous involvement. The affection may be confounded with benign tumors of the lacrimal gland (adenoma, adenofibroma) and especially with simple sclerotic hypertrophy (chronic dacryoadenitis) which it resembles even to the histological appearances. The diagnosis may be confirmed by inoculation into guinea-pigs. Treatment can be expectant, spontaneous regression being possible: The rational method, however, is extirpation.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Endothelium in the Healing of Aseptic Wounds in the Omentum of Rabbits.—(A continuation of recent interesting experimental investigations of the mononuclear wandering cell of endothelial origin.) FOOT (*Studies on Endothelial Reactions*, v. *Jour. Exper. Med.*, 1921, **34**, 625) has resulted in certain important findings which tend to upset our present conception of wound healing. The writer found that in the development of granulation tissue in the omentum in animals "vitally stained" by the use of a carbon suspension, there was active endothelial proliferation resulting in: (1) the formation of new capillaries from the existing capillaries; (2) the formation of vitally stained endothelial phagocytes; (3) the formation of cells bearing carbon granules (thus indicating their endothelial origin), but which also showed fibroglial and collagen fibrils. This third group was somewhat difficult to classify. In all essentials they were fibroblasts, except that they contained particles from the injected carbon suspension. This led the writer into a very attractive hypothesis regarding granulation tissue, namely, that both the endothelium of the vessels and the connective tissue of the part are stimulated in such a way that reversion to an embryonal character occurs. In this state it is apparent that connective tissue cells may be phagocytic for particulate substances, as has been claimed by some, and further, embryonal endothelial cells may even differentiate as fibroblasts under the stress of the need for tissue repair. The writer believes that under these conditions (wound repair) a mesenchyme is formed in which all three types occur, and that they are interchangeable when in the embryonal state. He believes that the endothelium furnishes by far the greater part of the mesenchymal tissue, basing this opinion on actual counts of mitoses in fixed tissue cells as compared to similar counts on vascular endothelium. The formation of collagen fibrils apparently independently of cellular activity is also reported. The writer considers further investigation of Baitsell's work in this line necessary. The nature of the experiments, in which silk sutures were employed, made possible a study of the foreign-body gaint cell, or endothelial syncytium, with the interesting findings that both fusion and nuclear division are probably responsible for the formation of these structures. Fusion has been observed and would seem from a study of the origin of the endothelial wandering cell to be the logical process. The writer has further corroborated this view by noting the breaking up into individual cells of syncytia, after the

silk stitch had been completely absorbed. But equally interesting in his finding (in two instances shown in photographs) of mitotic figures in syncytia. The mesothelial layer covering the omentum was never shown to give rise to phagocytes and simply covered the denuded surface, as does the epithelium in skin wounds.

Studies on the Nature of the Action of Non-specific Protein in Disease Processes. I. *Typhoid Protein (Dead Typhoid Bacilli and Soluble Toxin).*—Certain microörganisms, such as the diphtheria and tetanus bacillus, do their damage to body cells by a soluble toxin produced at the local site of infection, while others, such as the typhoid and influenza bacillus and the pneumococcus, wrought their havoc upon liberation of their endotoxin. COWIE and KEMPTON (*Jour. Med. Research*, 1921, **42**, 227) conducted a series of experiments as to whether the "sterilizing" changes which occur in the body after an intravenous injection of foreign protein may be explained on purely physical or physicochemical grounds. Guinea-pigs which received intravenous and subcutaneous injections of dead typhoid bacilli (300,000,000 to a 150-gram pig) showed a definite reaction which was of less severity than that seen in man. It was found that dead typhoid bacilli, after being in contact with diphtheria toxin at 37° C. for one hour, did not form a permanent union with the toxin or alter the toxic effect of the fatal doses of the toxin when introduced along with the toxin, subcutaneously, into guinea-pigs. There was not sufficient absorption or adsorption of the toxin to lessen the effect of the fatal dose when dead typhoid bacilli were allowed to remain in intimate contact with diphtheria toxin at 37° C. for two hours and then separated from the toxin by centrifugalization. Dead typhoid bacilli did not protect against a lethal dose of diphtheria toxin given one week after the last intravenous or subcutaneous injections or near the same time of the injections. Similarly, dead typhoid bacilli, where injected intravenously simultaneously with or on alternate days after the introduction of diphtheria toxin, furnished no protection to guinea-pigs against the toxin.

II. *Horse Serum and Soluble Toxin.*—In a second communication, COWIE and GREENTHAL (*Jour. Med. Research*, 1921, **42**, 261) called attention to the fact that 1 cc of normal horse serum, when injected subcutaneously or intravenously into guinea-pigs at the same time as diptheria toxin, would always protect against a fatal dose or even as high as eight fatal doses, while larger doses of the horse serum protected against larger doses of the diphtheria toxin, although the effect was not necessarily proportional. The highest protection was 15 M.L.D. with 3 cc of horse serum. The protecting power of the horse serum was found to reside in the protein portion rather than the alcoholic soluble fraction.

Effect of Blood from Immune Animals upon Transplantable Tumors.—Many investigators have reported conflicting conclusions concerning the effect of "immune" serum on transplantable tumors in various laboratory animals. KROSS (*Jour. Cancer Research*, 1921, **6**, 25) injected, intraperitoneally, one group of Marshall rats with blood

from August rats; a second group of Marshall rats with blood from normal Marshall rats and a third group with no blood. All three groups were then inoculated with grafts of 0.002 gm. of the Flexner rat carcinoma in the right axilla. The same procedure was instituted in the August rat, the immune Marshall rats being used as a source for the immune blood and the Jensen rat sarcoma being inoculated. It was observed that the transfused blood accelerated rather than retarded the development of the tumors as to both time and intensity of growth. The writer states that "if immune bodies do exist in animals that are refractory to tumor growth, they are not resident in the circulating blood." In order to determine whether the blood or other proteins injected acted as a food, a series of rats were injected, intraperitoneally and subcutaneously, with blood, and another series with egg white. One cc of each was administered every three days over a period of six weeks. All animals were then inoculated with the Jensen rat sarcoma. No appreciable difference was noted in the growth of the tumors in the inoculated rats or the controls, the writer believing that the blood did not act as nutriment.

An Inquiry into the Distribution of the Blood Groups in Patients Suffering from "Malignant Disease."—ALEXANDER (*British Jour. Exper. Path.*, 1921, **2**, 66) studied the blood groups of 50 patients with "malignant disease," a term including cases of carcinoma, sarcoma, rodent ulcer and leukemia, this last condition being regarded provisionally as a sarcoma of the hemopoietic system. The routine method was to test the patient's corpuscles against known Group II and III sera, a time limit of sixty seconds for the reading being maintained. As controls, the blood group was determined in 50 normal persons and in 125 cases with other diseases, notably tuberculosis, syphilis and tetanus. It was found that, while persons belonging to all four groups are liable to malignant disease, those in Groups I and III appear to be peculiarly susceptible, and the clinical type of disease is, as a rule, more malignant.

The Influence of Chaulmoogra Oil on the Tubercle Bacillus.—Although Walker and Sweeny found that the sodium salts of the total fatty acids of chaulmoogra oil (chaulmoograte) were highly bactericidal for the tubercle bacillus in vitro, KOLMER, DAVIS and JAGER (*Jour. Infect. Dis.*, 1921, **28**, 265) were unable to demonstrate any appreciable germicidal effect in vitro of undiluted chaulmoogra oil and dilutions in paraffin oil on a virulent strain of bovine tubercle bacilli when McMaster's technic was used. In a second series of experiments, it was found that undiluted and diluted chaulmoogra oil exerted no appreciable germicidal influence on B. tuberculosis when a vitro-vivo method, utilizing guinea-pigs, was employed. It was also learned that chaulmoogra oil in doses of 0.2 cc per 100 gm. of body weight administered by intramuscular injection at weekly intervals had little or no effect on the course of tuberculosis in infected guinea-pigs. The chaulmoogra oil was relatively nontoxic for the guinea-pigs.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Reinfection in Tuberculosis. Experimental Arrested Tuberculosis and Subsequent Infections.—"The observant student of the history of tuberculosis will be inclined to reflect that the problems concerning it have a way of recurring." BALDWIN and GARDNER (*Am. Rev. Tubere.*, 1921, **5**, 429) have been studying the question of reinfection in tuberculosis, with special reference to experimental arrested tuberculosis and subsequent infections. These authors state that it seems to them that the frequency of infection is one of the most important of modern problems in tuberculosis, and to it they have devoted their efforts. By frequency of infection is meant the actual number of implantations of tubercle bacilli received into the body from outside sources, not the metastatic spread of a preëxisting focus of tuberculosis; in short, exogenous reinfection as distinguished from endogenous spread by any or all ways, internal or external, but originating in the individual himself. The authors have taken a broad and philosophical view of the situation and summarized their results as follows: In the face of many complexities it is presumption to marshal the known facts into a law applicable to all cases of a disease exhibiting such great contrasts. The medical world seeks for a formula or creates one according to the degree of dogmatism of its author. Then comes a world war and its aftermath of disease and privation; the formula does not apply and confusion reigns again. It is indeed a disquieting thing to contemplate the reported large increase of tuberculosis in Europe and then point to the steady fall in mortality from this disease up to the war years as due to the suppression of the tubercle bacillus. Moreover the abrupt fall of the tuberculosis death-rate in this country since the influenza pandemic has puzzled those who predicted a large increase of tuberculosis following the war and the pandemic. Harmonizing these experiences presupposes more knowledge than we possess, yet not all is mystery. There is a period between the date of infection and the recognition of tuberculosis as a disease that is lost to us in too many cases. The symptoms are absent or too vague and fleeting for our present methods of detection. There are, it is true, the earliest hemoptyses without other symptoms, the definite pleurisies, not to mention the external forms of tuberculosis possible of early discovery. The postmortem not infrequently reveals a group of fairly early tubercles in the lung parenchyma and oftener well-marked tracheobronchial

involvement of uncertain age in individuals dying from other causes. These are not, by any means now at our command, connected with a definite period of time of infection unless we are to except children. There are primary infections, progressive and fatal at all ages. In the races recently brought into contact with tubercle bacilli the matter offers the simple explanation that there is no resting period once the infection had begun to spread. The elements of dosage and frequent cumulative infection must be considered in these cases because of the manner of life of the people. When acute primary tuberculosis is suspected in an adult of the white race and of cleanly habits there has been a tendency to assume an unusual virulence of the bacillus, ignoring the possible absence of resistance from lack of previous infection. Certain families have been devastated by acute tuberculosis where we should expect early infection, and, from the relative immunity thus acquired, a slower course of the disease. It must be remembered that not all the individuals in such families do in fact exhibit such acute forms of the disease, and some, perchance, escape altogether. These again are the puzzling contradictions. To return, therefore, to the main fact of universal infection, single or repeated, for an interpretation of all these variations. It is evident that successive infections do occur and that the first often modifies the course of the later ones. In comparison with the ease with which a primary infection is acquired the later inhaled and ingested bacilli are resisted more or less strongly by the relative "immunity from infection." In applying these principles to human tuberculosis many evidences of confirmation are noted which in the main are satisfactory. There are reasons to suspect mild infection both as to quantity and virulence, occurring infrequently but by a cumulative effect ultimately arousing the disease process. The earliest exogenous reinfections are probably often well resisted and may produce no noticeable symptoms. Good physiological functions combined with the immunity from infection tend to ward off further infection after adult age is reached. Should the conditions be otherwise than favorable, or the infection frequent or potent, disease results. The authors discuss the unlikelihood of massive infections by inhalation and the doubt about other ways of reinfection. From the very small quantities taken in at one time and the slow development of the disease they are inclined to the theory of cumulative infection during childhood and youth. The majority of individuals who are to develop pulmonary tuberculosis for the first time after the age of twenty have already acquired it to a degree. Were it possible to discover these potentially diseased cases who may or may not break down we believe that there would be but a small percentage not accounted for among the victims of tuberculosis in civilized countries. It is virtually impossible to associate many cases of clinical tuberculosis in adults with a recent exogenous source of infection, except under family exposure. Even in family disease, as is well known, the patient often develops the first recognized symptoms years after the death of the relative. Many similar observations might be brought forward to show the futility of trying to place the date of infection, except in those adults (either of primitive races or others) hitherto unexposed because of complete isolation. The town or city dweller is a survivor in the sense that he has reached maturity in the face of more or less inevitable exposure to

human and bovine infection. The result of wholesale physical examinations are impressive in the number of unsuspected pulmonary cases in fair health. What happens to many of these may be surmised from the increased mortality during the war and from the sanatorium records of relapse. Under strain and with an acute influenza, others have come to knowledge but are not yet recorded in the mortality tables. The steady decrease of tuberculosis for years antedating the great war has been variously interpreted, but from the revelations mentioned concerning the large number of undiscovered cases the authors state that the lessening of opportunities for infection has not been accomplished to the extent desired. Yet they are persuaded that the frequency and quantity are lessened. Meanwhile the standards of life had improved, tending to prevent both exogenous and endogenous additions to the already acquired war and its hardships, exposure and starvation. Thousands of arrested or partially arrested tuberculous persons have relapsed and their disease become progressive. Deaths were hastened, and together with influenza the work of years seemed wasted by the war. The amount of disease during the war attributable to reinfection cannot be estimated, but it is safe to say it was but little in the armies. With the crowding of the cities by workers and the combined strain we should frankly expect many new infections. The authors believe that the lesson to be learned and applied is that, hand in hand with efforts to safeguard the young from infection, more attention should be paid to safeguarding both young and old from disease. Without sputum and dairy hygiene the supply of dangerously infected young people will be kept up; without earlier diagnosis, education and favorable conditions of life for the prospective victims clinical tuberculosis will continue at an irreducible minimum.

A Work Chair to Prevent Fatigue. — EMMONS and GOLDTHWAIT (*Jour. Ind. Hygiene*, 1921, **3**, 154) illustrate and describe the common faults of seating in workrooms, offices, etc., and present a sturdy chair designed to give support to the small of the back while working at a desk or table and during intervals of relaxation. The chair described is for general use in most occupations in offices and work-rooms. The only adjustment to this chair is different lengths of legs. Especially adjusted chairs may still be necessary for special jobs or special individuals, but the adjustable chair often needs an adjustor. The chair has been successfully tested in an educational institution and in a factory for five years, and is enthusiastically endorsed by the managers.

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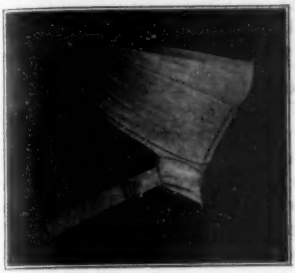

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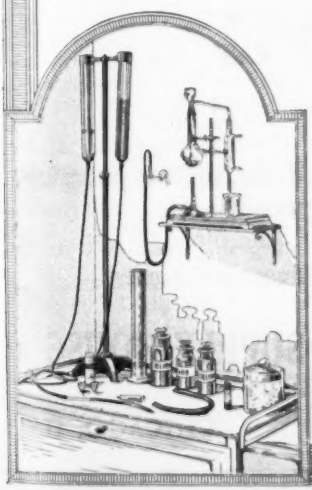

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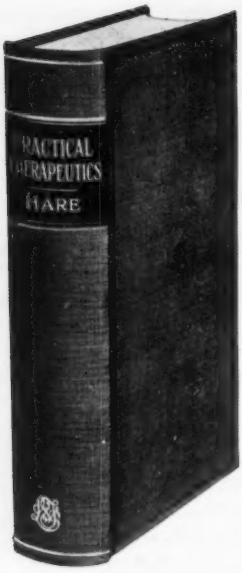

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Normal School of Physical Education
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